

Efficient One-Step Suzuki Arylation of Unprotected Halonucleosides using Water-Soluble Palladium Catalysts

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Experimental

General. 8-Bromo-2'-deoxyguanosine,¹ 8-bromo-2'-deoxyadenosine,² *t*-Bu-Pip-phos,³ DCPES,⁴ pyren-1-ylboronic acid,⁵ and TXPTS⁶ were prepared according to literature methods. Water and acetonitrile were combined and sparged for 15 minutes with nitrogen prior to use. Reactions were assembled in a nitrogen dry box in vials closed with screw-cap septa or round-bottomed flasks sealed with rubber septa. Reactions using TPPTS or TXPTS as ligand could also be assembled in air and degassed by sparging with nitrogen after addition of solvent. Reaction progress was analyzed by RP-HPLC (C-18 column, eluted with a gradient ranging from 10% MeOH in H₂O to 80% MeOH in H₂O, detection at 263 nm for adenosine and guanosine derivatives and 300 nm for uridine derivatives) or RP-TLC (C-18, 1:1 H₂O:MeOH eluent). High resolution mass spectra were obtained using FAB ionization.

General method for arylation of 8-BrdG and 8-BrG. Palladium acetate (2.2 mg, 0.01 mmol), TPPTS (14.8 mg, 0.025 mmol), sodium carbonate (80 mg, 0.75 mmol), 8-BrdG or 8-BrG (0.375 mmol), and arylboronic acid (0.45 mmol) were placed in a round-bottomed flask under nitrogen. Degassed 2:1 water:acetonitrile was added (3.5 mL) and the reaction heated in an oil bath at 80 °C until RP-TLC (1:1 water:methanol) showed complete conversion (2-4 hours). The reaction was diluted with ca. 20 mL of water and the pH adjusted to 6-7 using 10% aqueous HCl. The mixture was heated to dissolve precipitated solids and then allowed to cool to 0 °C and stand for several hours. The product was recovered as a microcrystalline solid.

8-Phenyl-2'-deoxyguanosine (4a).⁷ Using the general procedure, 8-BrdG (129.6 mg, 0.374 mmol) was coupled with phenylboronic acid (68.2 mg, 0.560 mmol). 8-PhdG (99.7 mg, 78%) was recovered as an off-white, microcrystalline solid from the reaction mixture after workup. ¹H NMR (360 MHz, DMSO-d₆): δ 10.8 (brs, 1H), 7.66-7.63 (m, 2H), 7.57-7.52 (m, 3H), 6.41 (brs, 2H), 6.07 (dd, *J* = 6.38, 8.20 Hz, 1H), 5.13 (d, *J* = 4.46 Hz, 1H), 4.97 (dd, *J* = 5.47, 6.38 Hz, 1H), 4.33 (m, 1H, 3'-H), 3.79-3.77

(m, 1H), 3.69-3.62 (m, 1H), 3.57-3.50 (m, 1H), 3.27-3.13 (m, 1H), 2.03 (ddd, $J = 1.73, 7.36, 12.97$ Hz, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 159.8, 155.1, 152.1, 146.3, 130.6, 129.2, 129.1, 128.6, 117.3, 88.1, 85.0, 71.4, 62.3, 36.9.

8-(4-Methylphenyl)-2'-deoxyguanosine (4b). Adduct **4b** was prepared using the general procedure, but on a larger scale. Coupling of 8-BrdG (266.6 mg, 0.770 mmol) and 4-tolylboronic acid (122.6 mg, 0.902 mmol) gave **4b** (267.8 mg, 97% yield) as a microcrystalline solid after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 10.74 (brs, 1H), 7.53 (d, $J = 8.18$ Hz, 2H), 7.34 (d, $J = 8.19$ Hz, 2H), 6.38 (brs, 2H), 6.05 (dd, $J = 6.70, 8.19$ Hz, 1H), 5.13 (d, $J = 4.46$ Hz, 1H), 4.98 (dd, $J = 5.21, 5.95$ Hz, 1H), 4.33 (m, 1H), 3.79-3.77 (m, 1H), 3.67-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.27-3.14 (m, 1H), 2.39 (s, 3H) 2.03 - 1.97 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.6, 152.9, 151.9, 147.2, 139.0, 129.1, 129.0, 127.5 117.1, 87.8, 84.6, 71.2, 65.1, 36.5, 20.9. High Resolution FAB-MS: Calculated for $\text{C}_{17}\text{H}_{19}\text{N}_5\text{O}_4 \cdot \text{Na}^+$: 380.1335. Found: 380.1342. Analysis: Calculated for $\text{C}_{17}\text{H}_{19}\text{N}_5\text{O}_4 \cdot \text{H}_2\text{O}$: C, 54.39; H, 5.64; N, 18.65. Found: C, 54.77; H, 5.24; N, 18.59.

8-(4-Hydroxymethylphenyl)-2'-deoxyguanosine (4c).⁸ Coupling of 8-BrdG (133.8 mg, 0.386 mmol) and 4-hydroxymethylphenylboronic acid (68.1 mg, 0.448 mmol) gave adduct **4c** after work up. The product was recovered as a fine powder (112.6 mg, 78% yield). ^1H NMR (360 MHz, DMSO- d_6): δ 10.73 (brs, 1H), 7.60 (d, $J = 8.01$ Hz, 2H), 7.47 (d, $J = 8.63$ Hz, 2H), 6.38 (brs, 2H), 6.06 (dd, $J = 6.78, 8.01$ Hz, 1H), 5.30 (t, $J = 5.85$ Hz, 1H), 5.13 (d, $J = 3.70$ Hz, 1H), 4.98 (dd, $J = 5.24, 6.47$ Hz, 1H), 4.58 (d, $J = 5.54$ Hz), 4.33 (m, 1H), 3.79-3.77 (m, 1H), 3.67-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.27-3.14 (m, 1H), 2.03 - 1.97 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.6, 152.9, 151.9, 147.1, 144.0, 128.9, 128.6, 126.5, 117.1, 87.8, 84.6, 71.2, 62.5, 62.1, 36.5. High Resolution FAB-MS: Analysis: Calculated for $\text{C}_{17}\text{H}_{19}\text{N}_5\text{O}_5 \cdot \text{Na}^+$: 396.1284. Found: 396.1281. Calculated for $\text{C}_{17}\text{H}_{19}\text{N}_5\text{O}_5$: C, 54.69; H, 5.13; N, 18.75. Found: C, 54.48; H, 5.09; N, 18.84.

8-(4-Methoxyphenyl)-2'-deoxyguanosine (4d). Coupling of 8-BrdG (128.6 mg, 0.371 mmol) and 4-methoxyphenylboronic acid (68.3 mg, 0.449 mmol) gave adduct **4d** after work up. The product was recovered as a fine powder (123.5 mg, 89% yield). ¹H NMR (360 MHz, DMSO-d₆): δ 10.70 (brs, 1H), 7.58 (d, *J* = 8.63 Hz, 2H), 7.09 (d, *J* = 8.63 Hz, 2H), 6.35 (brs, 2H), 6.04 (dd, *J* = 6.78, 8.02 Hz, 1H), 5.11 (d, *J* = 4.31 Hz, 1H), 4.96 (dd, *J* = 5.55, 6.16 Hz, 1H), 4.33 (m, 1H), 3.83 (s, 3H) 3.79-3.77 (m, 1H), 3.67-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.27-3.14 (m, 1H), 2.03 - 1.97 (m, 1H). ¹³C NMR (90.6 MHz, DMSO-d₆): δ 161.3, 159.9, 156.0, 152.0, 146.0, 130.5, 123.0, 117.3, 114.0, 88.1, 85.1, 71.6, 62.5, 55.3, 37.0. High Resolution FAB-MS: Calculated for C₁₇H₁₉N₅O₅•Na⁺: 396.1284. Found: 396.1285. Analysis: Calculated for C₁₇H₁₉N₅O₅•H₂O: C, 52.19; H, 5.41; N, 17.89. Found: C, 52.79; H, 5.38; N, 17.89.

8-(4-Fluorophenyl)-2'-deoxyguanosine (4e). Coupling of 8-BrdG (135.3 mg, 0.391 mmol) and 4-fluorophenylboronic acid (62.9 mg, 0.450 mmol) gave adduct **4e** after work up. The product was recovered as a fine powder (101.9 mg, 72% yield). ¹H NMR (360 MHz, DMSO-d₆): δ 10.76 (brs, 1H), 7.71 (dd, ³*J*_{H-F} = 5.36 Hz, ³*J*_{H-H} = 8.05 Hz, 2H), 7.38 (dd, ³*J*_{H-F} = 8.72 Hz, ³*J*_{H-H} = 8.72 Hz, 2H), 6.43 (brs, 2H), 6.04 (dd, *J* = 7.38, 7.38 Hz, 1H), 5.13 (d, *J* = 3.70 Hz, 1H), 4.95 (dd, *J* = 5.62, 6.70 Hz, 1H), 4.33 (m, 1H), 3.79-3.77 (m, 1H), 3.67-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.27-3.14 (m, 1H), 2.03 - 1.97 (m, 1H). ¹³C NMR (90.6 MHz, DMSO-d₆): δ 162.6 (d, ¹*J*_{C-F} = 246.68 Hz), 159.6, 153.0, 152.0, 146.1, 131.4 (d, *J* = 8.90 Hz), 126.9 (d, *J* = 2.54 Hz), 117.0, 115.6 (d, *J* = 21.62 Hz), 87.8, 84.5, 71.1, 62.0, 37.0. High Resolution FAB-MS: Calculated for C₁₆H₁₆FN₅O₄•Na⁺: 384.1084. Found: 384.1070. Analysis: Calculated for C₁₆H₁₆FN₅O₄•(H₂O)_{0.75}: C, 51.41; H, 4.71; N, 18.68. Found: C, 51.20; H, 4.64; N, 19.20.

8-(4-Carboxyphenyl)-2'-deoxyguanosine, sodium salt (4f). 8-BrdG (130.0 mg, 0.375 mmol) and 4-carboxyphenylboronic acid (76.8 mg, 0.463 mmol) were coupled under the standard conditions. Once the reaction had reached completion, the reaction mixture adjusted to pH 7 with 10% HCl and loaded

onto 10g of C-18 SPE material. The column was eluted with several volumes of water followed by 20% MeOH in water until the **4f** had eluted completely. The combined fractions were concentrated to give the product as a glassy solid (119.0 mg, 77% yield). ^1H NMR (360 MHz, DMSO- d_6): δ 12.50 (vbrs, 1H), 8.03 (d, $J = 8.19$ Hz, 2H), 7.60 (d, $J = 8.19$ Hz, 2H), 7.19 (brs, 2H), 6.13 (t, $J = 7.45$ Hz, 1H), 5.22 (brs, 1H), 4.34 (brs, 1H), 4.12 (brs, 1H), 3.79-3.77 (m, 1H), 3.67-3.61 (m, 1H), 3.57-3.52 (m, 1H), 3.27-3.14 (m, 1H), 2.03 - 1.97 (m, 1H). ^1H NMR (360 MHz, D_2O): δ 7.95 (d, $J = 8.02$ Hz, 2H), 7.59 (d, $J = 8.02$ Hz, 2H), 6.21 (t, $J = 7.40$ Hz, 1H), 4.64-4.61 (m, 1H), 4.07-4.04 (m, 1H), 3.87 (dd, $J = 3.09, 12.33$ Hz, 1H), 3.82 (dd, $J = 4.63$ Hz, 12.75 Hz, 1H), 3.03 (ddd, $J = 7.57, 7.20, 14.33$ Hz, 1H), 2.25 (ddd, $J = 3.08, 6.37, 14.27$ Hz, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 169.6, 157.7, 154.1, 152.1, 146.8, 140.6, 130.8, 129.1, 128.2, 117.1, 87.8, 84.6, 71.2, 62.2, 48.6, 36.7. High Resolution FAB-MS (negative mode): Calculated for $\text{C}_{17}\text{H}_{16}\text{N}_5\text{O}_6^-$: 386.1101. Found: 386.1103.

8-Phenylguanosine (8a).⁹ Using the general procedure, 8-BrG (136.2 mg, 0.376 mmol) was coupled with phenylboronic acid (54.2 mg, 0.447 mmol). 8-PhG (89.4 mg, 66%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 10.76 (s, 1H), 7.69-7.63 (m, 2H), 7.57-7.49 (m, 3H), 6.39 (s, 2H), 5.64 (d, $J = 6.17$ Hz, 1H), 5.37 (d, $J = 6.17$ Hz, 1H), 5.08-5.00 (m, 2H), 4.97 (d, $J = 5.55$ Hz, 1H), 4.08 (dd, $J = 5.24, 10.48$ Hz, 1H), 3.83 (q, $J = 4.32$ Hz, 1H), 3.71-3.64 (m, 1H), 3.59-3.51 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.6, 153.1, 152.0, 147.4, 130.0, 129.4, 129.1, 128.6, 117.1, 88.9, 85.8, 70.6, 70.3, 62.1. High resolution FAB-MS: Calculated for $\text{C}_{16}\text{H}_{18}\text{N}_5\text{O}_5^+$: 360.1308. Found: 360.1317.

8-(4-Methoxyphenyl)guanosine (8d). Using the general procedure, 8-BrG (135.1 mg, 0.373 mmol) was coupled with 4-methoxyphenylboronic acid (67.6 mg, 0.445 mmol). Adduct **8d** (100.7 mg, 69%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 10.76 (s, 1H), 7.59 (d, $J = 8.02$, 2H), 7.09 (d, $J = 8.63$, 2H), 6.37 (brs, 2H), 5.62 (d, $J = 6.78$, 1H), 5.36 (d $J =$

6.78, 1H), 5.04 (m, 3H), 4.07 (brs, 1H), 3.83 (brm, 1H), 3.55 (brm, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 160.1, 156.6, 153.0, 151.9, 147.5, 130.6, 122.4, 114.1, 88.9, 85.8, 70.6, 70.2, 62.1, 55.3. Two of the aromatic ring carbons overlapped in the ^{13}C NMR spectrum. High resolution FAB-MS: Calculated for $\text{C}_{17}\text{H}_{20}\text{N}_5\text{O}_6^+$: 390.1414. Found: 390.1404.

8-(4-Fluorophenyl)guanosine (8e). Using the general procedure, 8-BrG (137.5 mg, 0.380 mmol) was coupled with 4-fluorophenylboronic acid (60.4 mg, 0.431 mmol). Adduct **8e** (94.9 mg, 66%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 10.80 (s, 1H), 7.71 (dd, $J = 5.85, 7.40$ Hz, 2H), 7.38 (t, $J = 8.94$ Hz, 2H), 6.44 (s, 2H), 5.60 (d, $J = 6.78$ Hz, 1H), 5.40 (d, $J = 6.17$ Hz, 1H), 5.11-4.96 (m, 3H), 4.09-4.04 (brm, 1H), 3.86-3.81 (brm, 1H), 3.71-3.63 (m, 1H), 3.59-3.51 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 162.7 (d, $J = 246.9$ Hz), 156.7, 153.2, 152.0, 146.5, 131.5 (d, $J = 8.33$ Hz), 126.6 (d, $J = 4.16$ Hz), 117.1, 115.7 (d, $J = 20.8$ Hz), 88.9, 85.8, 70.5, 70.3, 62.0. High resolution FAB-MS: Calculated for $\text{C}_{16}\text{H}_{17}\text{N}_5\text{O}_5\text{F}^+$: 378.1214. Found: 378.1229.

General Method for Arylation of 8-BrdA, 8-BrA, and 5-IdU. Palladium acetate (2.2 mg, 0.01 mmol), TPPTS (11.5 mg, 0.02 mmol), sodium carbonate (80 mg, 0.75 mmol), halonucleoside (0.375 mmol), and arylboronic acid (0.425 mmol) were placed in a round-bottomed flask under nitrogen. Degassed 2:1 water:acetonitrile was added (3.5 mL) and the reaction was heated in an oil bath at 80 °C until RP-TLC (1:1 water:methanol) or HPLC showed completed conversion (2-4 hours). The reaction was diluted with ca. 20 mL of water and the pH adjusted to 7 using 10% aqueous HCl. The solution was purified by loading onto a column of reverse phase silica, eluted with a gradient ranging from 100% water to 100% methanol.

8-Phenyl-2'-deoxyadenosine (5a). Using the general procedure, 8-BrdA (122.3 mg, 0.371 mmol) was coupled with phenylboronic acid (51.9 mg, 0.428 mmol). 8-PhdA (105.8 mg, 87%) was recovered as a white, microcrystalline solid from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO-

d_6): δ 8.15 (s, 1H), 7.71 (t, $J = 3.08$ Hz, 2H), 7.61 (d, $J = 3.70$ Hz, 3H), 7.45 (s, 2H), 6.15 (t, $J = 7.40$ Hz, 1H), 5.57 (dd, $J = 3.70, 8.63$ Hz, 1H), 5.24 (d, $J = 4.32$ Hz, 1H), 4.46 (s, 1H), 3.90-3.85 (brm, 1H), 3.73-3.66 (m, 1H), 3.57-3.49 (m, 1H), 2.15 (dd, $J = 6.16, 13.56$ Hz, 1H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.2, 152.0, 150.5, 149.9, 130.1, 129.7, 129.5, 128.8, 119.2, 88.4, 85.7, 71.5, 62.3, 59.8, 37.2. High Resolution FAB-MS: Calculated for $\text{C}_{16}\text{H}_{18}\text{N}_4\text{O}_3^+$: 328.1410. Found: 328.1410.

8-(*p*-Tolyl)-2'-deoxyadenosine (5b). Using the general procedure 8-BrdA (129.6 mg, 0.393 mmol) was coupled with *p*-tolylboronic acid (61.6 mg, 0.453 mmol). **5b** (120.0 mg, 90%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 8.14 (s, 1H), 7.61 (d, $J = 8.02$, 2H), 7.61 (d, $J = 7.39$, 4H), 6.14 (dd, $J = 6.16, 8.63$, 1H), 5.55 (brdd, 1H), 5.22 (brs, 1H), 4.45 (brs, 1H), 3.87 (brd, 1H), 3.70 (m, 1H), 3.53 (m, 1H), 2.42 (s, 3H), 2.13 (ddd, $J = 1.85, 5.86, 13.6$, 1H, 2'-H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.1, 151.9, 150.6, 149.9, 139.9, 129.3, 126.8, 119.1, 88.4, 85.7, 71.5, 62.3, 37.2, 21.0. Two of the aromatic carbons overlap at 129.3 ppm. High resolution FAB-MS: Calculated for $\text{C}_{17}\text{H}_{20}\text{N}_5\text{O}_3^+$: 342.1566. Found: 342.1546.

8-(4-Hydroxymethylphenyl)-2'-deoxyadenosine (5c).⁸ Using the general procedure, 8-BrdA (124.2 mg, 0.376 mmol) was coupled with 4-hydroxymethylphenylboronic acid (65.0 mg, 0.428 mmol). **5c** (122.1 mg, 91%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 8.14 (s, 1H), 7.67 (d, $J = 8.63$ Hz, 2H), 7.53 (d, $J = 7.40$ Hz, 2H), 7.42 (s, 2H), 6.15 (dd, $J = 6.16, 8.63$ Hz), 5.57 (dd, $J = 3.70, 8.63$ Hz, 1H), 5.35 (t, $J = 5.55$ Hz, 1H), 5.22 (d, $J = 3.70$ Hz, 1H), 4.61 (d, $J = 5.55$ Hz, 2H), 4.45 (brs, 1H), 3.89-3.85 (brm, 1H), 3.74-3.66 (m, 1H), 3.58 (m, 1H), 2.14 (m, 1H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.2,

151.9, 150.6, 149.9, 144.8, 129.3, 127.9, 126.6, 119.2, 88.4, 85.8, 71.5, 62.5, 62.4, 38.8. High resolution FAB-MS: Calculated for $C_{17}H_{20}N_5O_4^+$: 358.1515. Found: 358.1513.

8-(4-Methoxyphenyl)-2'-deoxyadenosine (5d). Using the general procedure, 8-BrdA (117.8 mg, 0.357 mmol) was coupled with 4-methoxyphenylboronic acid (64.7 mg, 0.426 mmol). Adduct **5d** (110.7 mg, 87%) was recovered from the reaction mixture after workup. 1H NMR (360 MHz, DMSO- d_6): δ 8.13 (s, 1H), 7.66 (d, $J = 8.63$ Hz, 2H), 7.38 (s, 2H), 7.15 (d, $J = 9.25$ Hz, 2H), 6.15 (dd, $J = 6.17$, 8.63 Hz, 1 H), 5.58-5.51 (bm, 1H), 5.22 (bs, 1H), 4.46 (bs, 1H), 3.85 (s, 4H), 3.73-3.66 (m, 1H), 3.57-3.48 (m, 1H), 3.17 (d, $J = 4.93$, 1H), 2.16-2.09 (m, 1H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 160.6, 156.0, 151.7, 150.5, 149.9, 131.0, 121.8, 119.1, 114.2, 88.4, 85.7, 71.5, 62.4, 55.4, 37.1. High Resolution FAB-MS: Calculated for $C_{17}H_{20}N_5O_4^+$: 358.1515. Found: 358.1496.

8-(Pyren-1-yl)-2'-deoxyadenosine (5g). Using the general procedure, 8-BrdA (33.0 mg, 0.100 mmol) was coupled with pyren-1-ylboronic acid (36.8 mg, 0.151 mmol). Product **5g** (30.5 mg, 68%) was recovered from the reaction mixture after workup. 1H NMR (360 MHz, DMSO- d_6): δ 8.50 – 8.00 (m, 9 H), 7.96 (d, $J = 9.24$ Hz, 1H), 7.55 (brs, 2H), 5.81 (m, 1H), 5.70 (brs, 1H), 5.04 (brs, 1H), 4.32 (brs, 1H), 3.72 (brs, 1H), 3.67-3.62 (m, 1H), 3.50-3.46 (m, 1H), 2.08-2.04 (m, 1H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.9, 152.6, 150.0, 149.9, 132.7, 131.4, 130.8, 130.6, 129.4, 128.7, 127.8, 127.7, 127.3, 126.7, 126.5, 125.5, 125.1, 124.6, 124.3, 124.1, 120.2, 89.2, 86.8, 72.2, 63.1, 38.8.

8-Phenyladenosine (6a).¹⁰ Using the general procedure, 8-BrA (129.6 mg, 0.375 mmol) was coupled with phenylboronic acid (56.0 mg, 0.462 mmol). 8-PhA (111.8 mg, 87%) was recovered from the reaction mixture after workup. 1H NMR (360 MHz, DMSO- d_6): δ 8.16 (s, 1H), 7.76 (q, $J = 3.29$ Hz, 2H), 7.60 (t, $J = 3.09$, 3H), 7.49 (s, 2H), 5.76 (brd, $J = 6.78$, 2H), 5.53-5.36 (brs, 1H), 5.18 (dd, $J =$

5.24, 7.40 Hz, 1H), 4.19-4.15 (m, 1H), 3.96-3.92 (m, 1H), 3.74-3.67 (m, 1H), 3.60-3.51 (brm, 1H), one proton masked by residual water in sample. ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 156.2, 152.0, 150.9, 149.8, 130.1, 129.7, 129.4, 128.7, 119.1, 89.1, 86.7, 71.2, 71.1, 62.3. High resolution FAB-MS: Calculated for $\text{C}_{16}\text{H}_{18}\text{N}_5\text{O}_4^+$: 344.1359. Found: 344.1380.

8-(4-Methoxyphenyl)adenosine (6d).¹¹ Using the general procedure, 8-BrA (130.8 mg, 0.378 mmol) was coupled with 4-methoxyphenylboronic acid (76.5 mg, 0.503 mmol). **6d** (121.3 mg, 85%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 8.14 (s, 1H), 7.70 (d, $J = 8.63$ Hz, 2H), 7.47 (brs, 2H), 7.15 (d, $J = 8.63$ Hz, 2H), 5.85 (dd, $J = 3.09, 9.25$ Hz, 1H), 5.76 (d, $J = 7.40$ Hz, 1H), 5.50 (d, $J = 6.17$ Hz, 1H), 5.22-5.14 (brq, 2H), 4.19-4.15 (brm, 1H), 3.96-3.92 (brm, 1H), 3.85 (s, 3H), 3.78-3.66 (m, 1H), 3.59-3.44 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 162.3, 158.5, 150.0, 136.9, 129.1, 125.4, 113.6, 113.3, 87.5, 84.4, 70.3, 61.0, 55.1. High resolution FAB-MS: Calculated for $\text{C}_{17}\text{H}_{20}\text{N}_5\text{O}_5^+$: 374.1464. Found: 374.1469.

8-(4-Fluorophenyl)adenosine (6e).¹¹ Using the general procedure, 8-BrA (130.3 mg, 0.377 mmol) was coupled with 4-fluorophenylboronic acid (65.7 mg, 0.469 mmol). **6e** (135.9 mg, 99.9%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 8.16 (s, 1H), 7.81 (dd, $J = 5.55, 8.63$ Hz, 2H), 7.54 (brs, 2H), 7.45 (t, $J = 8.88$ Hz, 2H), 5.83 (dd, $J = 3.70, 9.25$ Hz, 1H), 5.72 (d, $J = 6.78$ Hz, 1H), 5.50 (brd, 1H), 5.21-6.13 (brm, 2H), 4.17 (brs, 1H), 3.95 (brs, 1H), 3.74-3.67 (m, 1H), 3.60-3.51 (m, 1H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 163.1 ($J = 248.3$ Hz), 156.3, 152.1, 149.9 ($J = 16.7$ Hz), 132.1, 132.0, 125.9, 119.1, 115.9 ($J = 22.2$ Hz), 89.1, 86.8, 71.3, 71.1, 62.3. High resolution FAB-MS: Calculated for $\text{C}_{16}\text{H}_{17}\text{N}_5\text{O}_4\text{F}^+$: 362.1265. Found: 362.1253.

5-Phenyl-2'-deoxyuridine (7a).¹² Using the general procedure, 5-IdU (134.4 mg, 0.380 mmol) was coupled with phenylboronic acid (53.8 mg, 0.444 mmol). 5-PhdU (91.7 mg, 79%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 11.0 (s, 1H), 8.17 (s, 1H), 7.55

(d, $J = 7.4$ Hz, 2H), 7.38-7.25 (m, 3H), 6.24 (t, $J = 6.48$ Hz, 1H), 5.26 (brs, 1H), 5.11 (brs, 1H), 4.32-4.26 (m, 1H), 3.81 (q, $J = 3.08$ Hz, 1H), 3.65-3.54 (m, 2H), 2.28-2.11 (m, 2H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 162.8, 150.4, 137.9, 133.5, 128.1, 127.9, 127.0, 113.5, 87.5, 84.5, 70.3, 61.0, 40.1.

5-(4-Methoxyphenyl)-2'-deoxyuridine (7d).¹³ Using the general procedure, 5-IdU (221.2 mg, 0.625 mmol) was coupled with 4-methoxyphenylboronic acid (120.5 mg, 0.793 mmol). **7d** (171.6 mg, 82%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 11.0 (s, 1H), 8.11 (s, 1H), 7.48 (d, $J = 8.63$ Hz, 2H), 6.93 (d, $J = 8.63$ Hz, 2H), 6.24 (t, $J = 6.78$ Hz, 1H), 5.26 (brs, 1H), 5.10 (brs, 1H), 4.31-4.25 (brm, 1H), 3.83-3.79 (brm, 1H), 3.76 (s, 3H), 3.66-3.53 (brm, 2H), 2.28-2.10 (m, 2H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 163.0, 158.4, 150.5, 136.8, 129.0, 125.8, 113.5, 113.3, 87.7, 84.4, 70.25, 61.0, 55.1, one peak obscured by solvent.

5-(4-Fluorophenyl)-2'-deoxyuridine (7e). Using the general procedure, 5-IdU (134.2 mg, 0.379 mmol) was coupled with 4-fluorophenylboronic acid (63.5 mg, 0.454 mmol). **7d** (111.9 mg, 92%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 11.0 (brs, 1H), 8.19 (s, 1H), 7.59 (dd, $J = 8.01$ Hz, 5.55 Hz, 2H), 7.19 (t, $J = 8.63$ Hz, 2H), 6.23 (t, $J = 6.78$ Hz, 1H), 5.26 (s, 1H), 5.12 (s, 1H), 4.29 (brs, 1H), 3.83-3.79 (m, 1H), 3.67-3.54 (m, 2H), 2.30-2.11 (m, 2H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 162.5 (d, $J = 44.4$ Hz), 160.0, 150.0, 137.9, 129.9 (d, $J = 8.32$ Hz), 129.6 (d, $J = 4.16$ Hz), 115.0, 114.8, 112.5, 87.5, 84.5, 70.1, 60.9, one peak obscured by solvent.

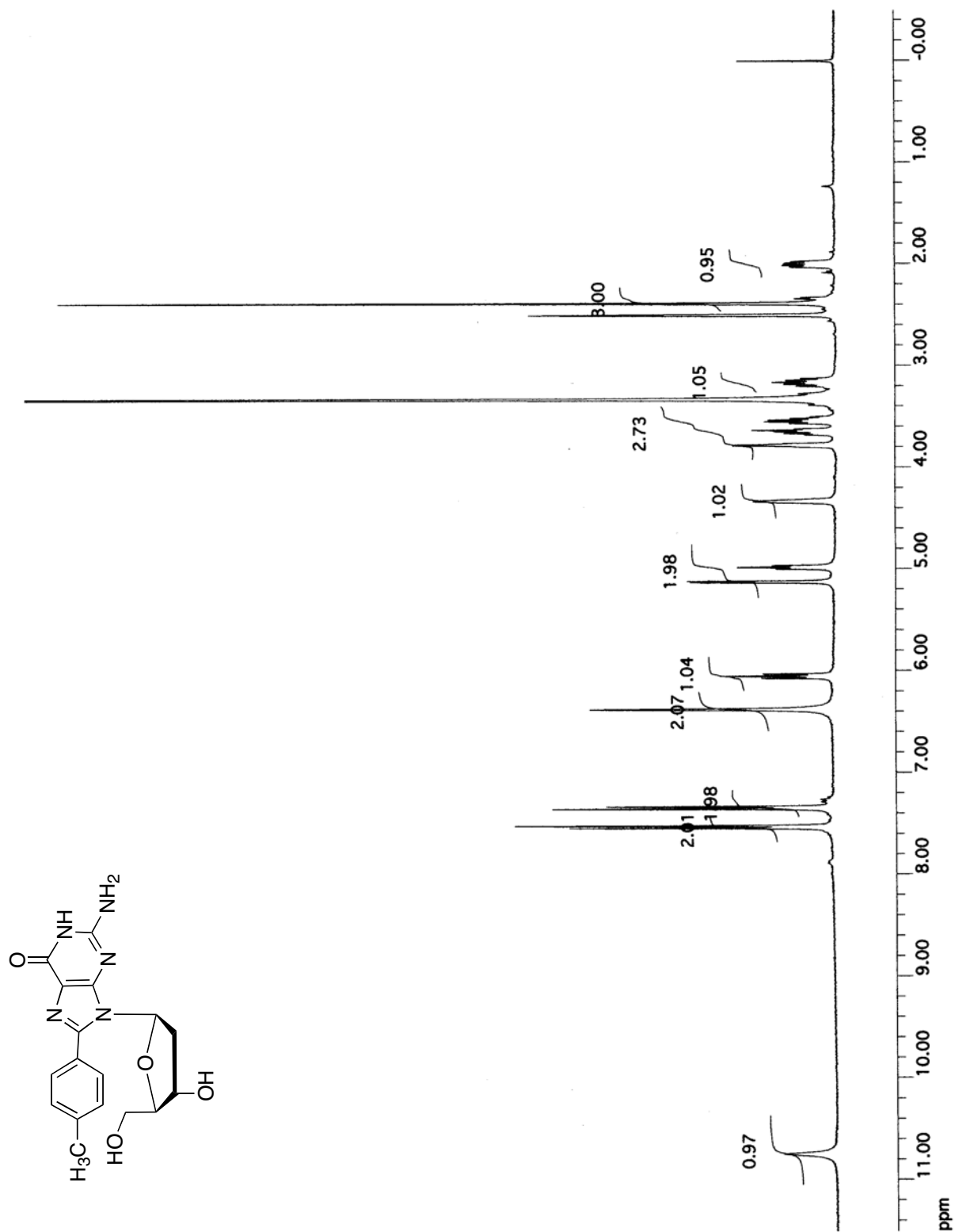
5-(2-Thienyl)-2'-deoxyuridine (7h).¹⁴ Using the general procedure, with the exception of using TXPTS (26.0 mg, 0.040 mmol) instead of TPPTS, 5-IdU (137.6 mg, 0.389 mmol) was coupled with 2-thienylboronic acid (**3h**, 56.6 mg, 0.442 mmol). **7h** (64.7 mg, 54%) was recovered from the reaction mixture after workup. ^1H NMR (360 MHz, DMSO- d_6): δ 10.8 (brs, 1H), 8.45 (s, 1H), 7.43 (d, $J = 4.93$ Hz, 1H), 7.38 (d, $J = 3.70$ Hz, 1H), 7.04 (dd, $J = 5.35, 3.70$ Hz, 1H), 6.22 (t, $J = 6.47$ Hz, 1H), 5.29 (brs,

2H), 4.31 (brs, 1H), 3.84 (q, $J = 3.08$ Hz, 1H), 3.73-3.60 (m, 2H), 2.27-2.13 (M, 2H). ^{13}C NMR (90.6 MHz, DMSO- d_6): δ 162.1, 150.0, 135.5, 134.4, 126.3, 125.4, 122.2, 108.3, 87.5, 84.8, 70.0, 60.9, 40.4.

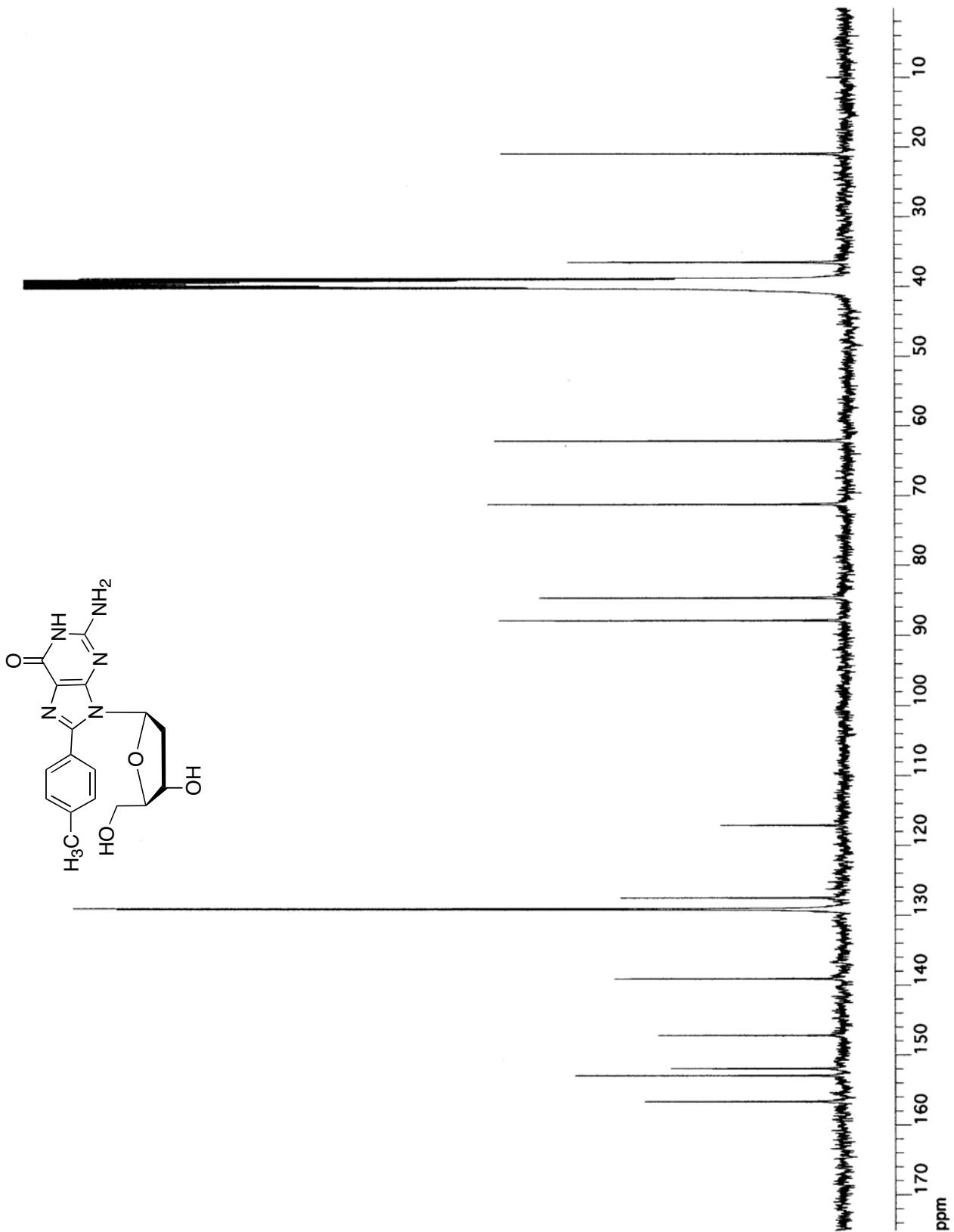
General procedure for couplings at room temperature using TXPTS/Pd(OAc) $_2$. Palladium acetate (2.2 mg, 0.01 mmol), TXPTS (13.0 mg, 0.02 mmol), sodium carbonate (80 mg, 0.75 mmol), halonucleoside (0.375 mmol), and arylboronic acid (0.425 mmol) were placed in a round-bottomed flask under nitrogen. Degassed 2:1 water : acetonitrile was added (3.5 mL) and the reaction was stirred at room temperature until complete. Work up and purification was carried out as described above.

General procedure for couplings in water using TXPTS/Pd(NO $_3$) $_2$. Palladium nitrate (2.3 mg, 0.01 mmol), TXPTS (13.0 mg, 0.02 mmol), sodium carbonate (80 mg, 0.75 mmol), halonucleoside (0.375 mmol), and arylboronic acid (0.425 mmol) were placed in a round-bottomed flask under nitrogen. Degassed water was added (3.5 mL) and the reaction was stirred at room temperature until complete. Work up and purification was carried out as described above.

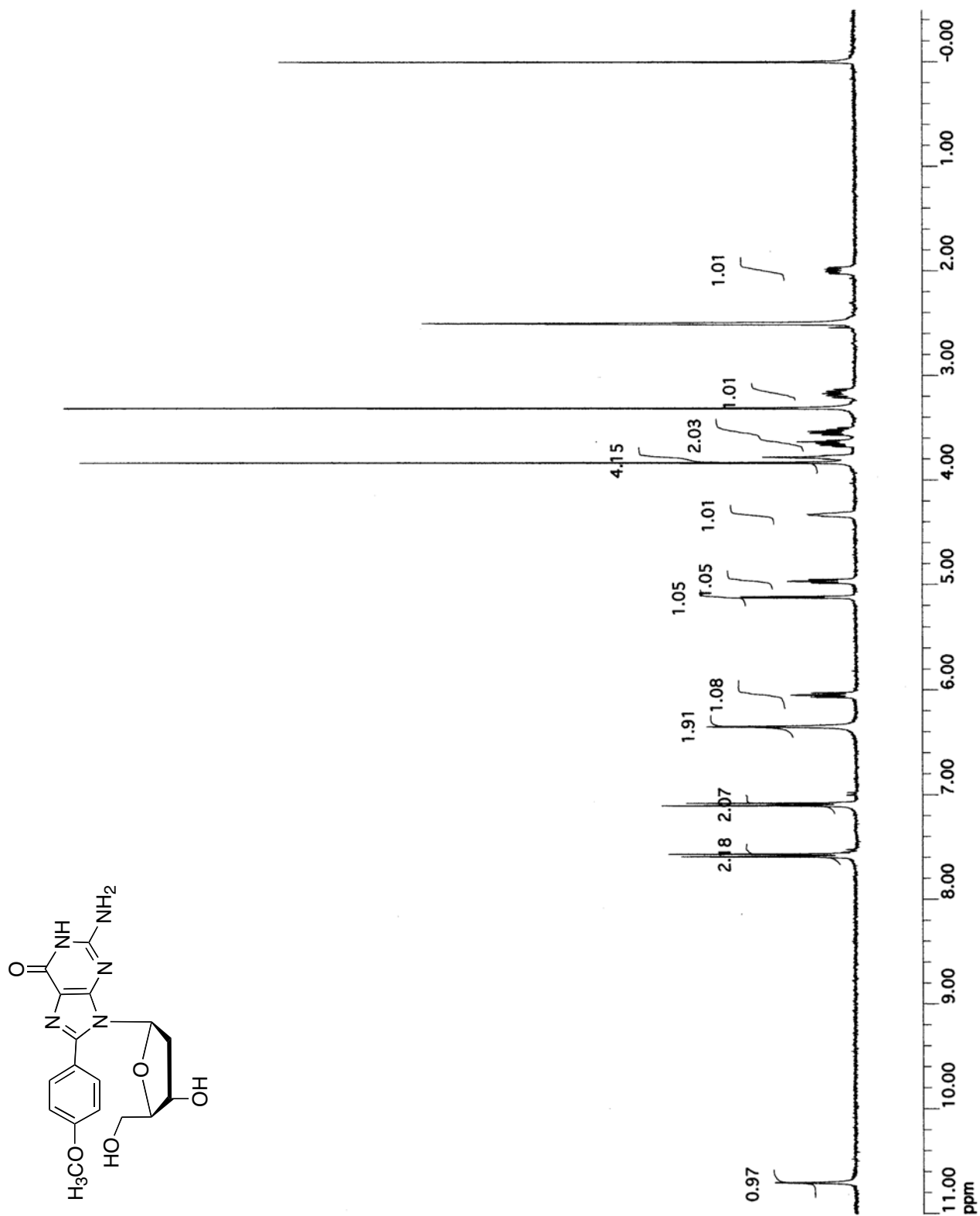
NMR Spectra



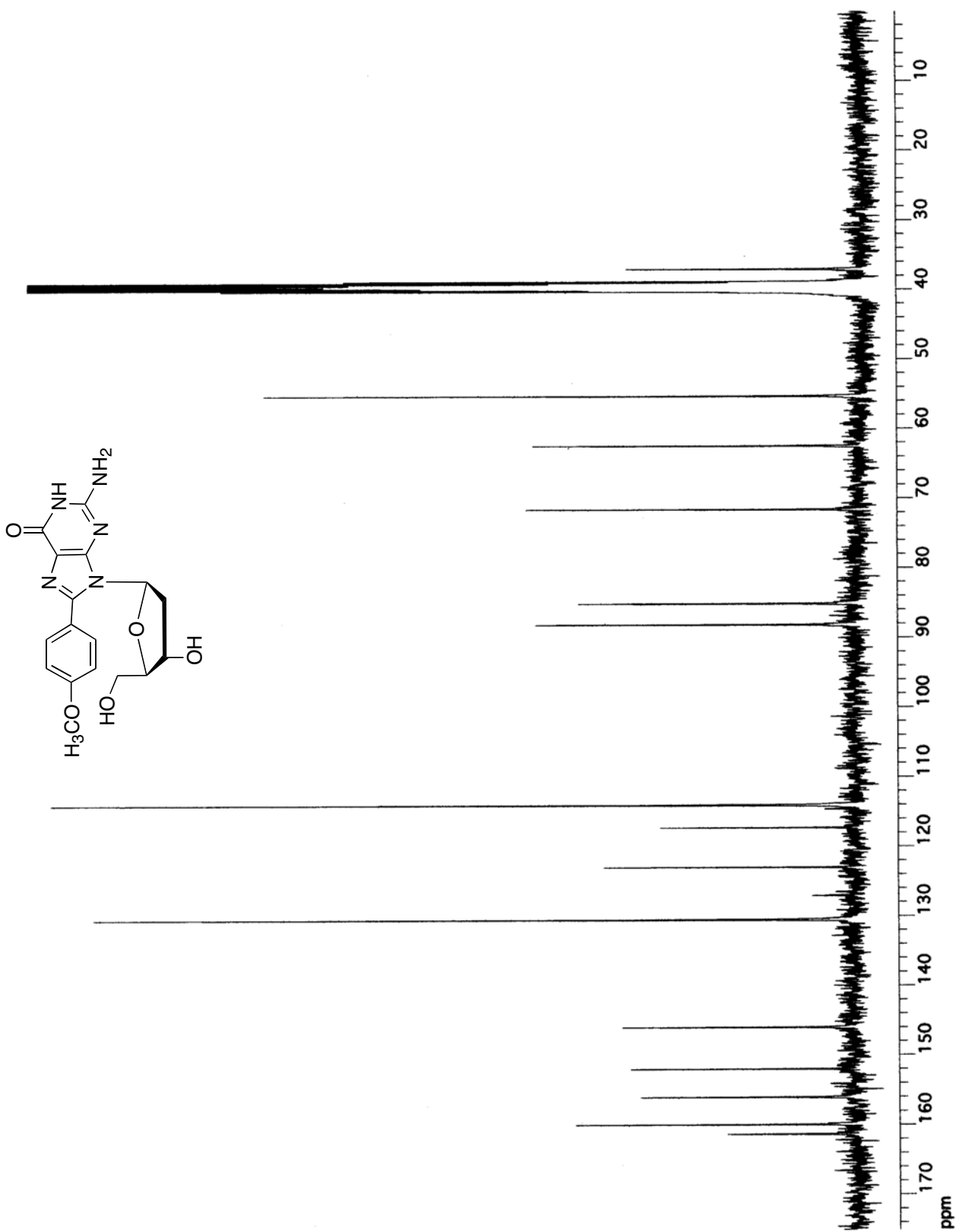
¹H NMR spectrum of 8-(4-tolyl)-2'-deoxyguanosine (**4b**)



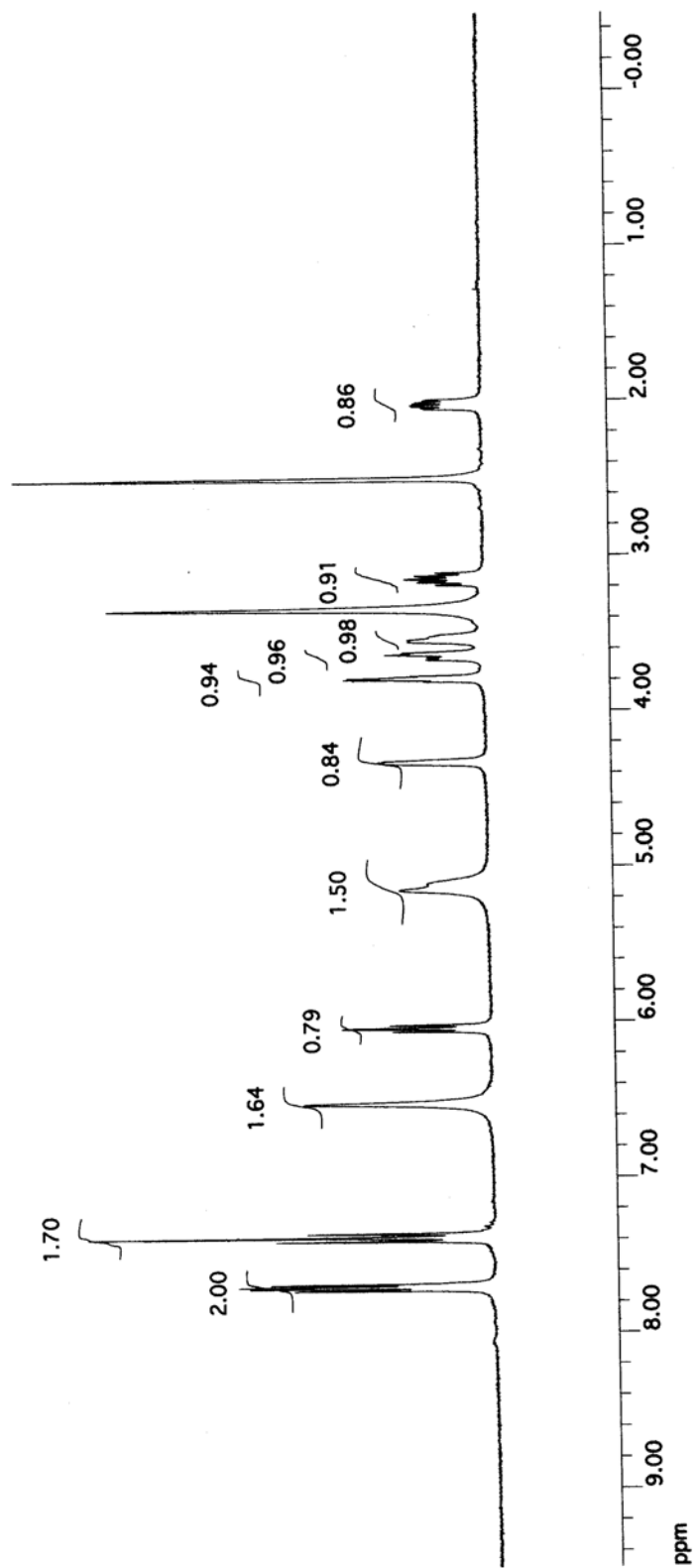
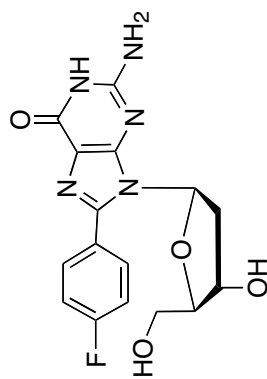
^{13}C NMR spectrum of 8-(4-tolyl)-2'-deoxyguanosine (**4b**)



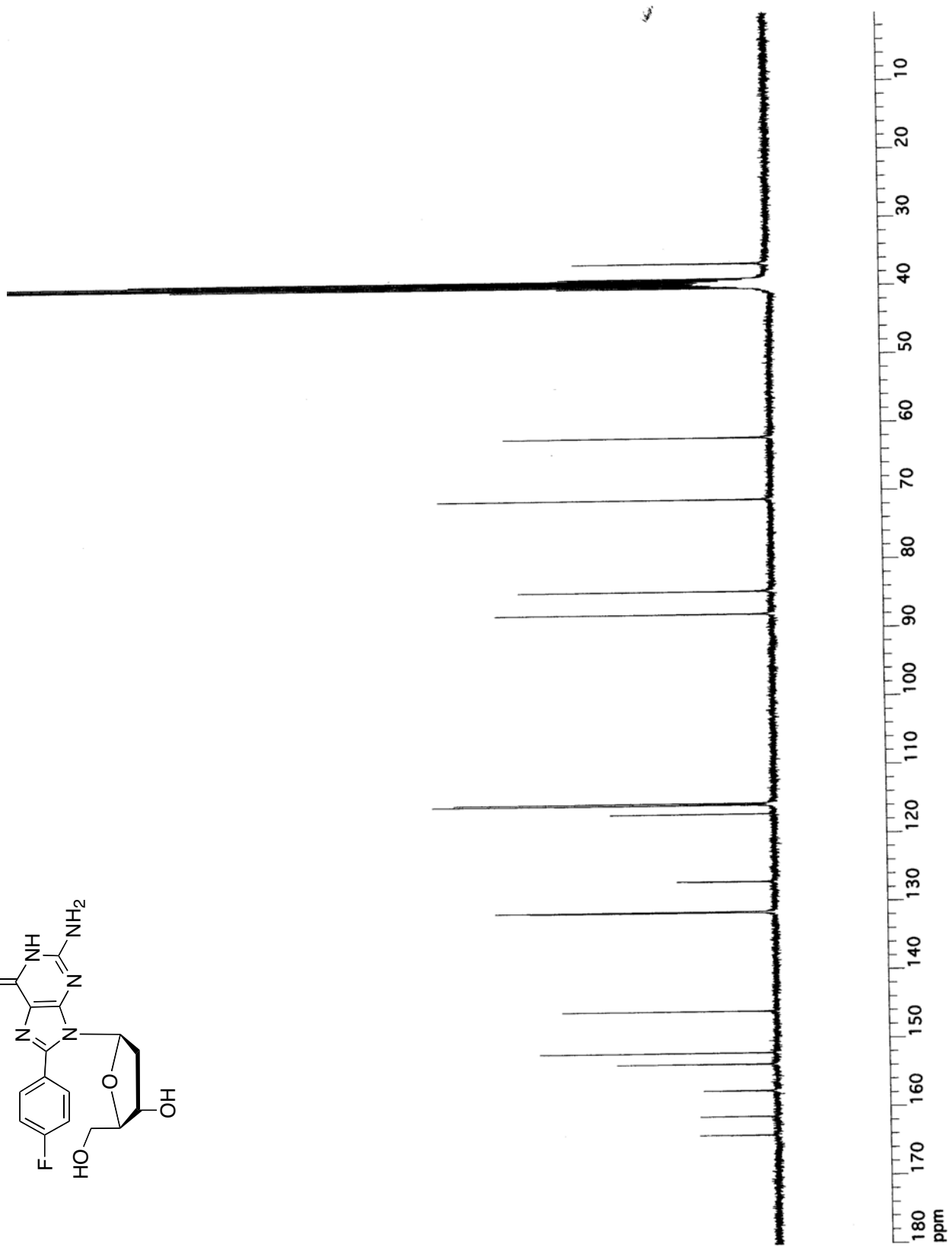
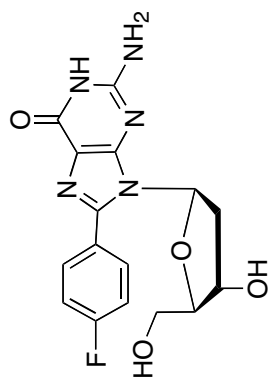
¹H NMR spectrum of 8-(4-methoxyphenyl)-2'-deoxyguanosine (**4d**)



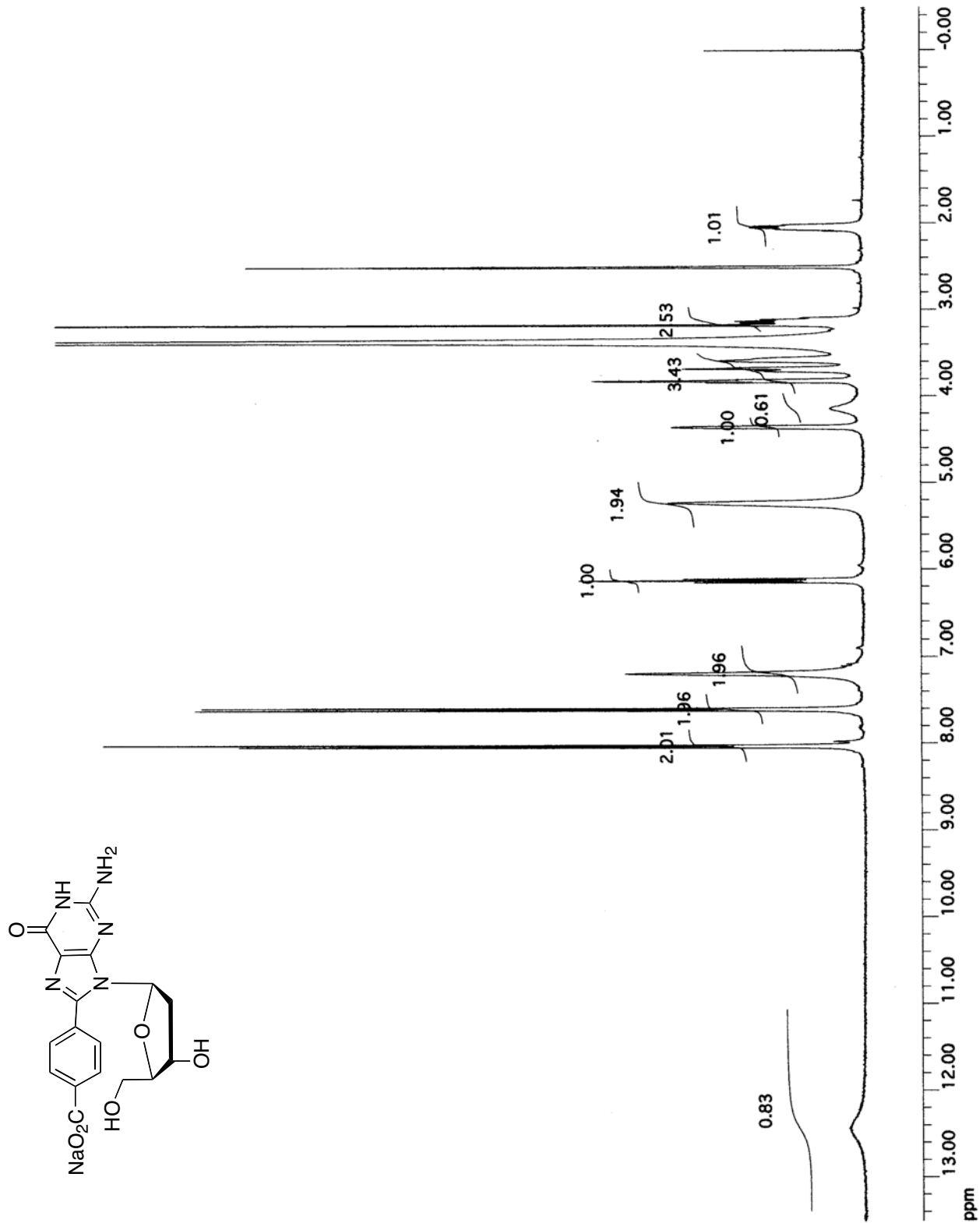
^{13}C NMR of 8-(4-methoxyphenyl)-2'-deoxyguanosine (**4d**)



¹H NMR of 8-(4-fluorophenyl)-2'-deoxyguanosine (4e)

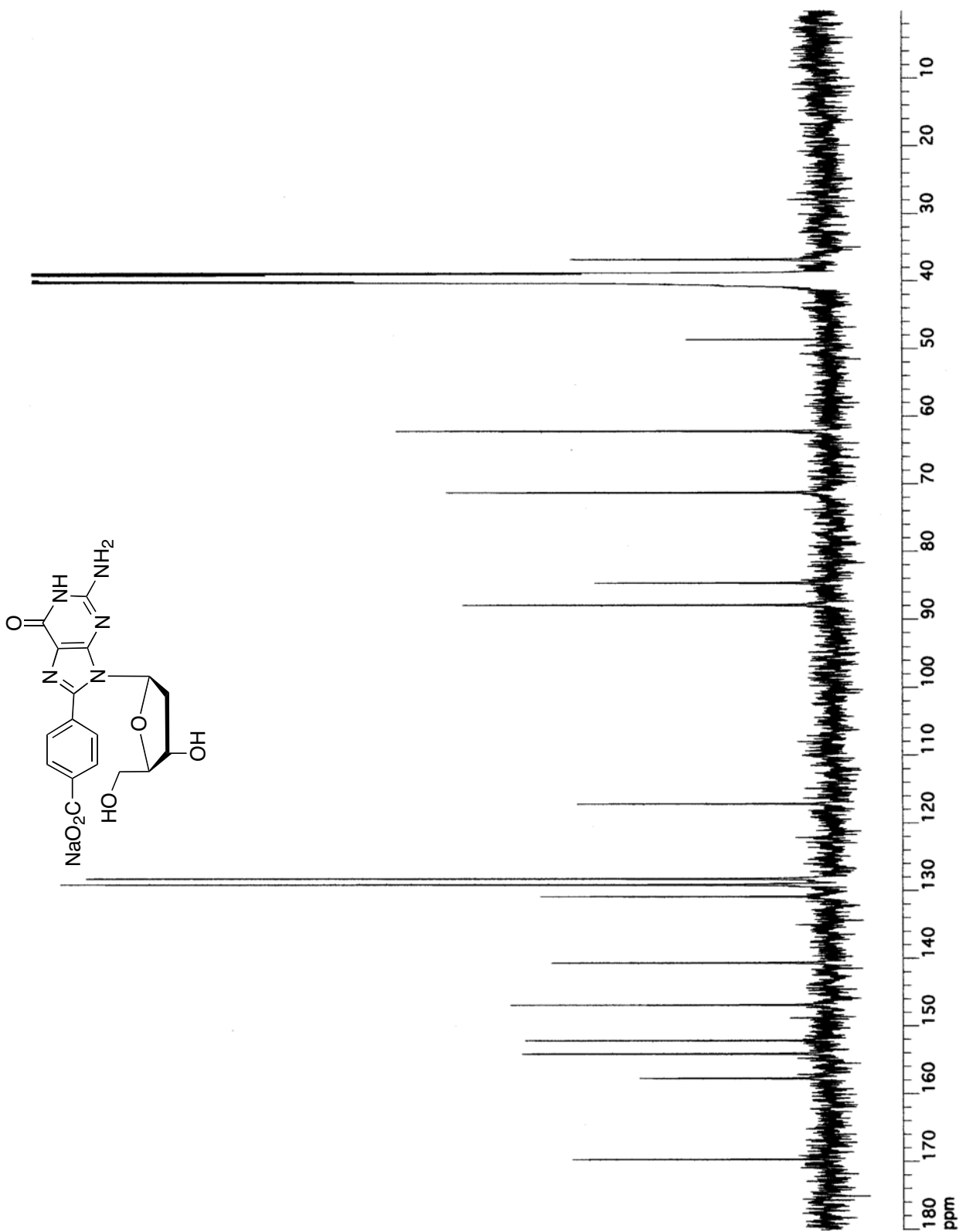


^{13}C NMR of 8-(4-fluorophenyl)-2'-deoxyguanosine (4e)

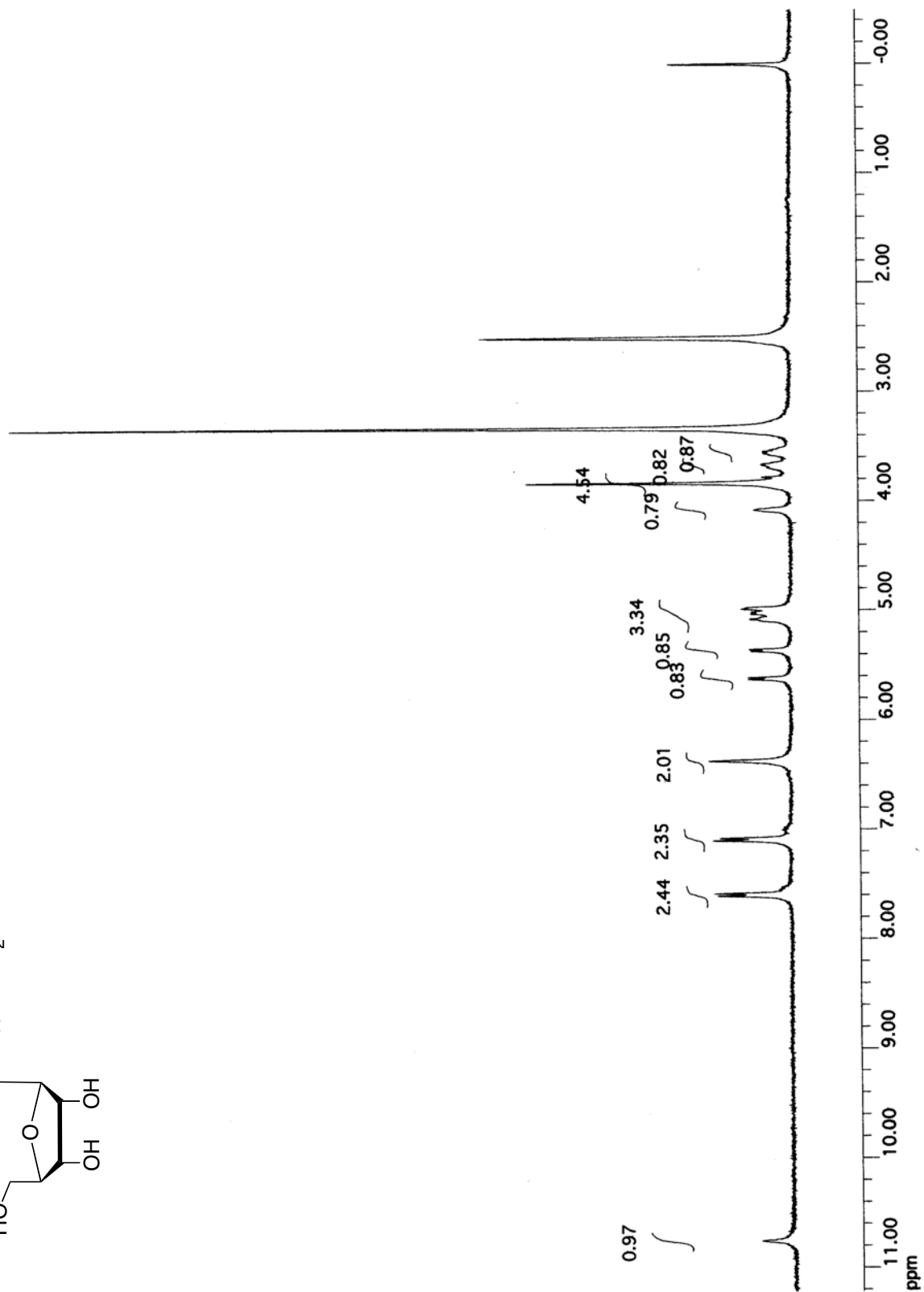
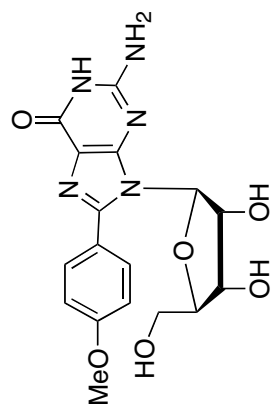


¹H NMR of 8-(4-carboxyphenyl)-2'-deoxyguanosine (**4f**)

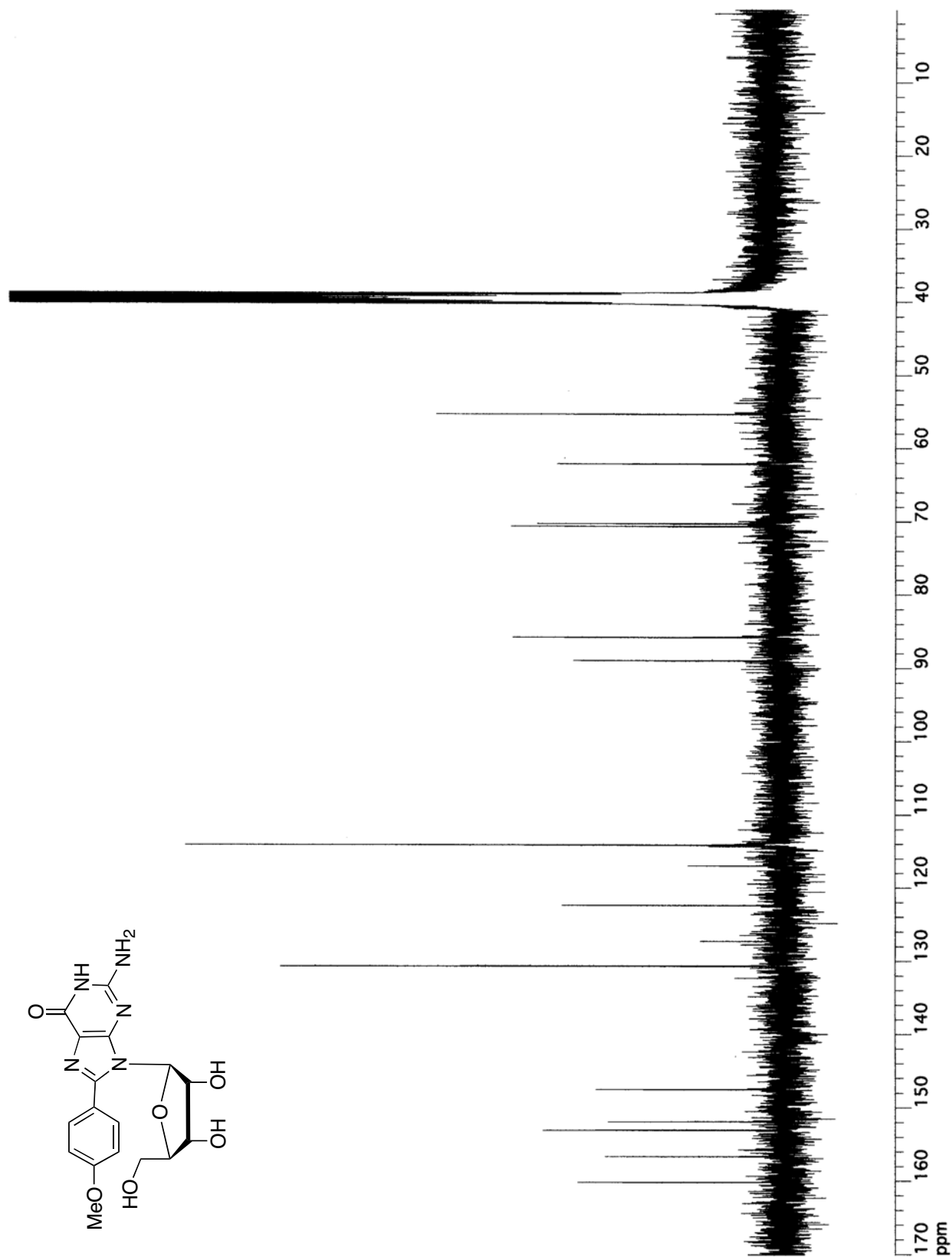
Residual methanol observed at 3.18 ppm.



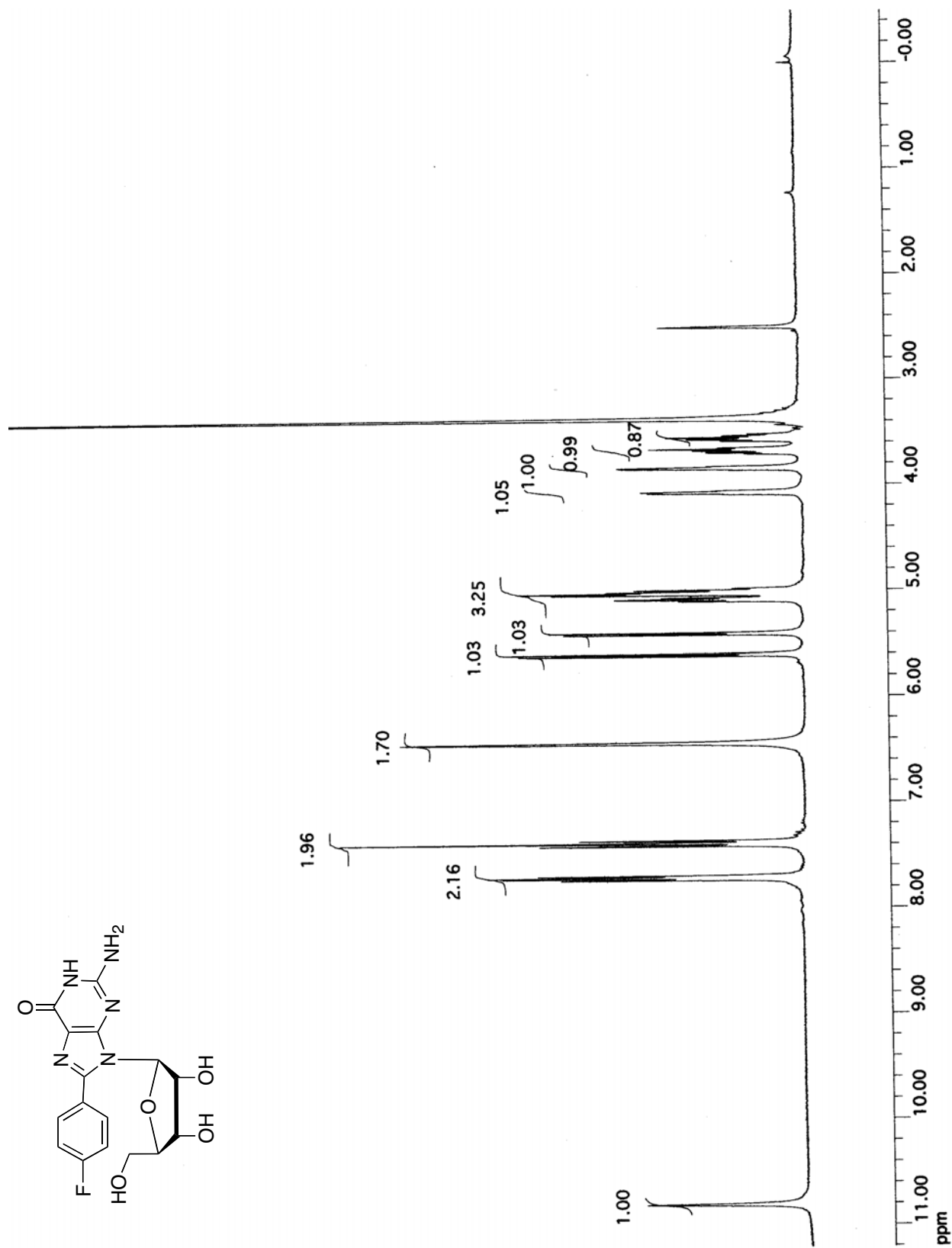
^{13}C NMR of 8-(4-carboxyphenyl)-2'-deoxyguanosine (4f)
Residual methanol observed at 48.5 ppm.



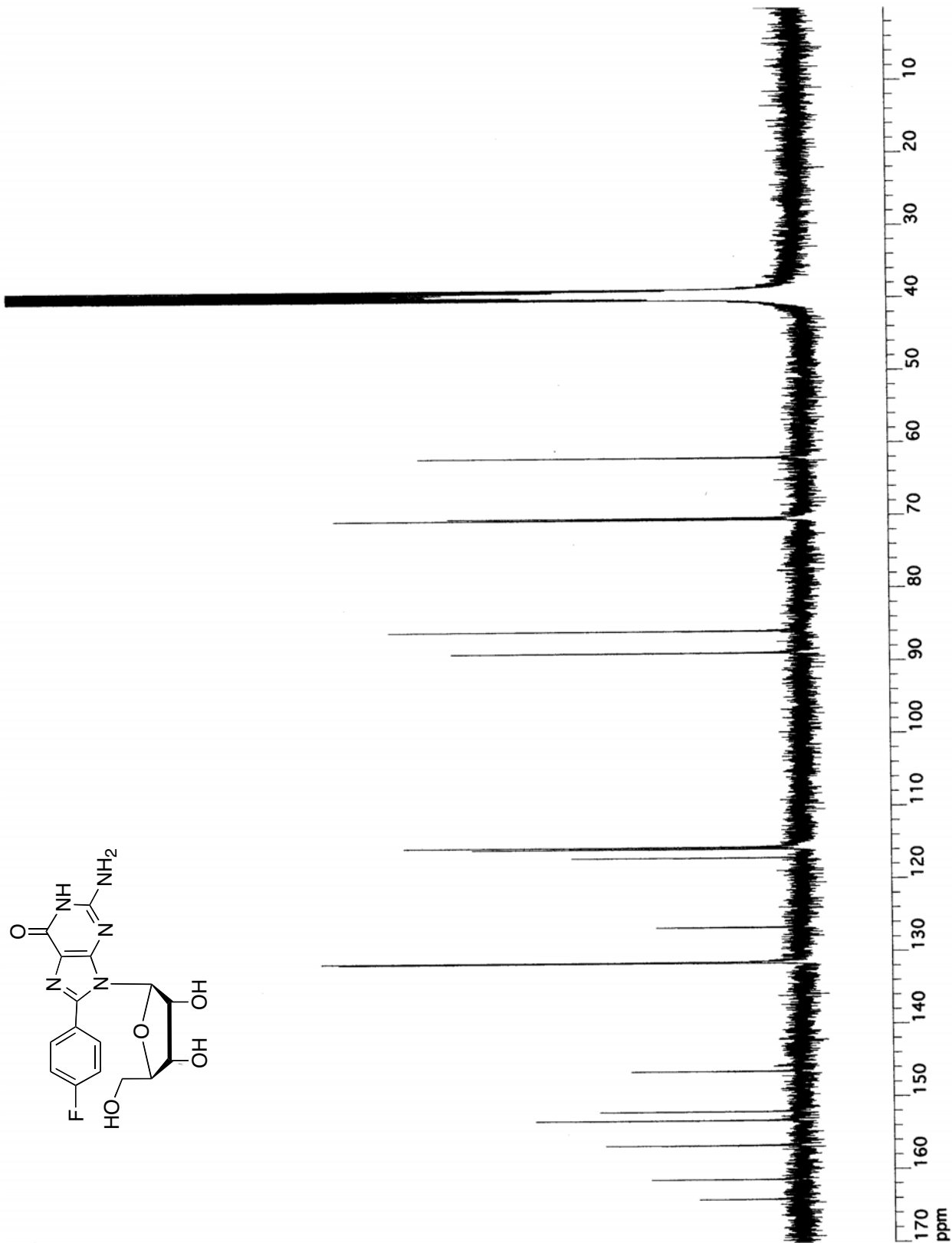
^1H NMR spectrum of 8-(4-methoxyphenyl)guanosine (**8d**)



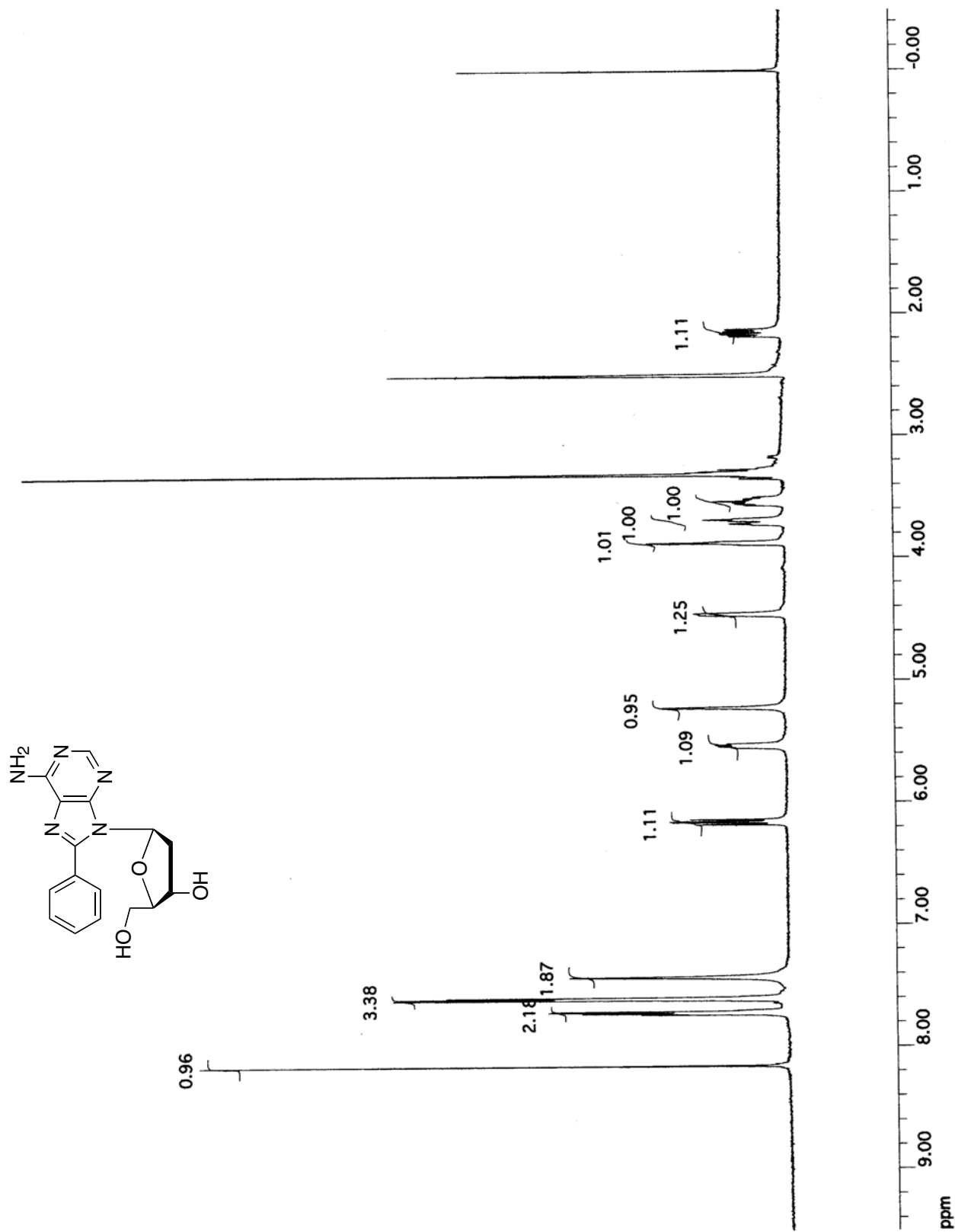
¹³C NMR spectrum of 8-(4-methoxyphenyl)guanosine (**8d**)



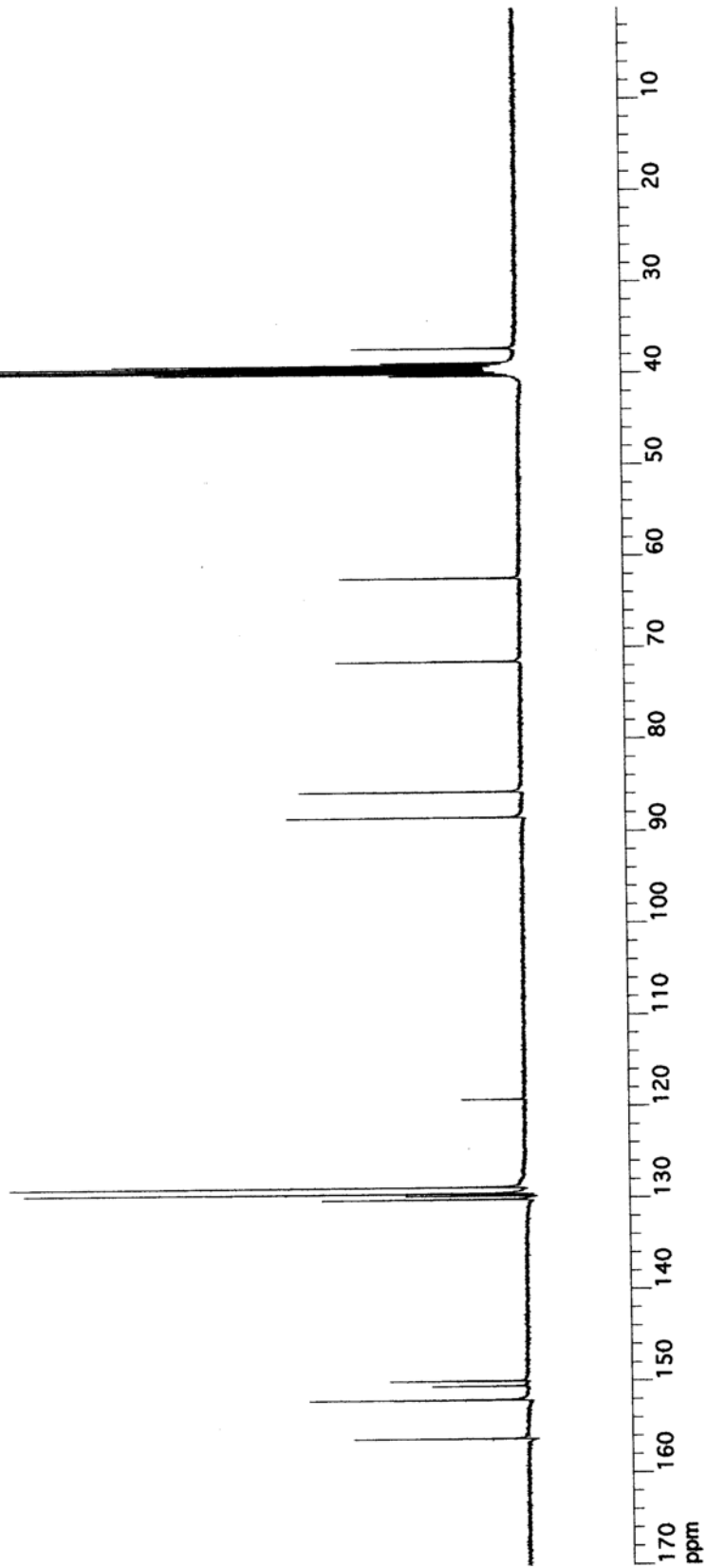
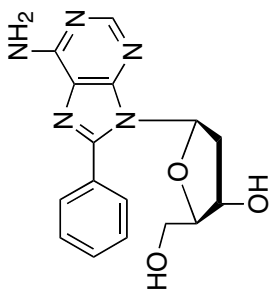
¹H NMR spectrum of 8-(4-fluorophenyl)guanosine (8e)



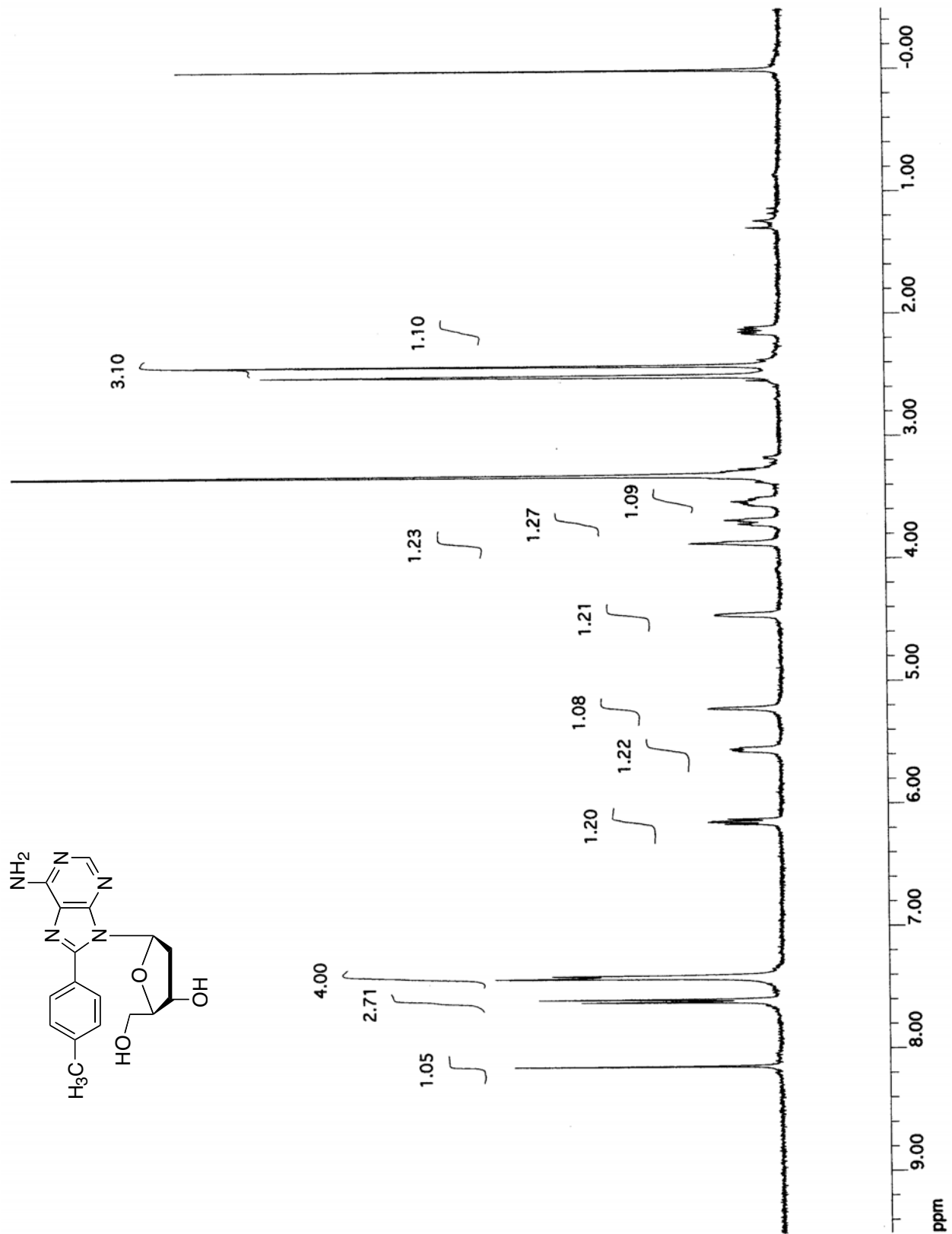
¹³C NMR spectrum of 8-(4-fluorophenyl)guanosine (8e)



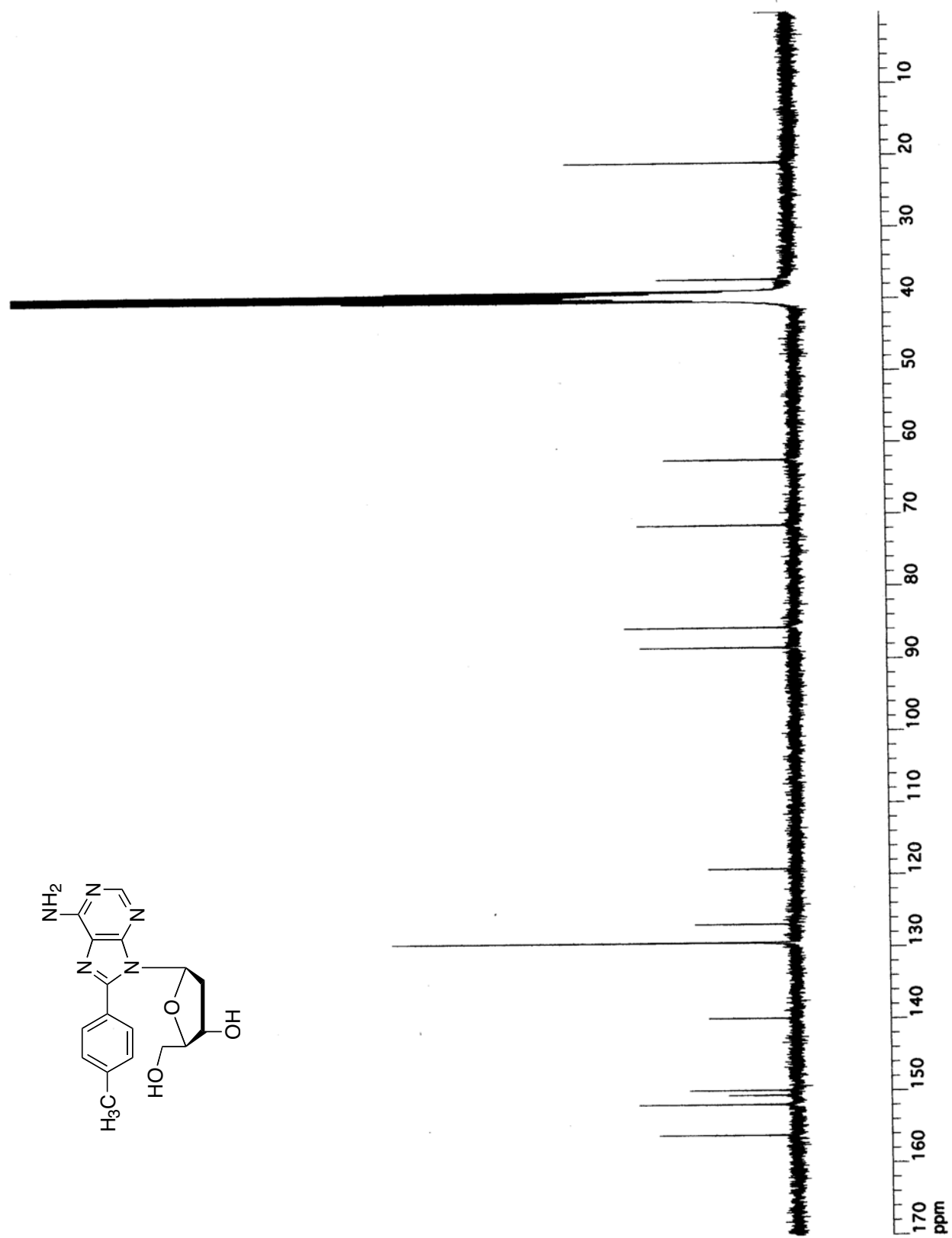
¹H NMR of 8-phenyl-2'-deoxyadenosine (**5a**)



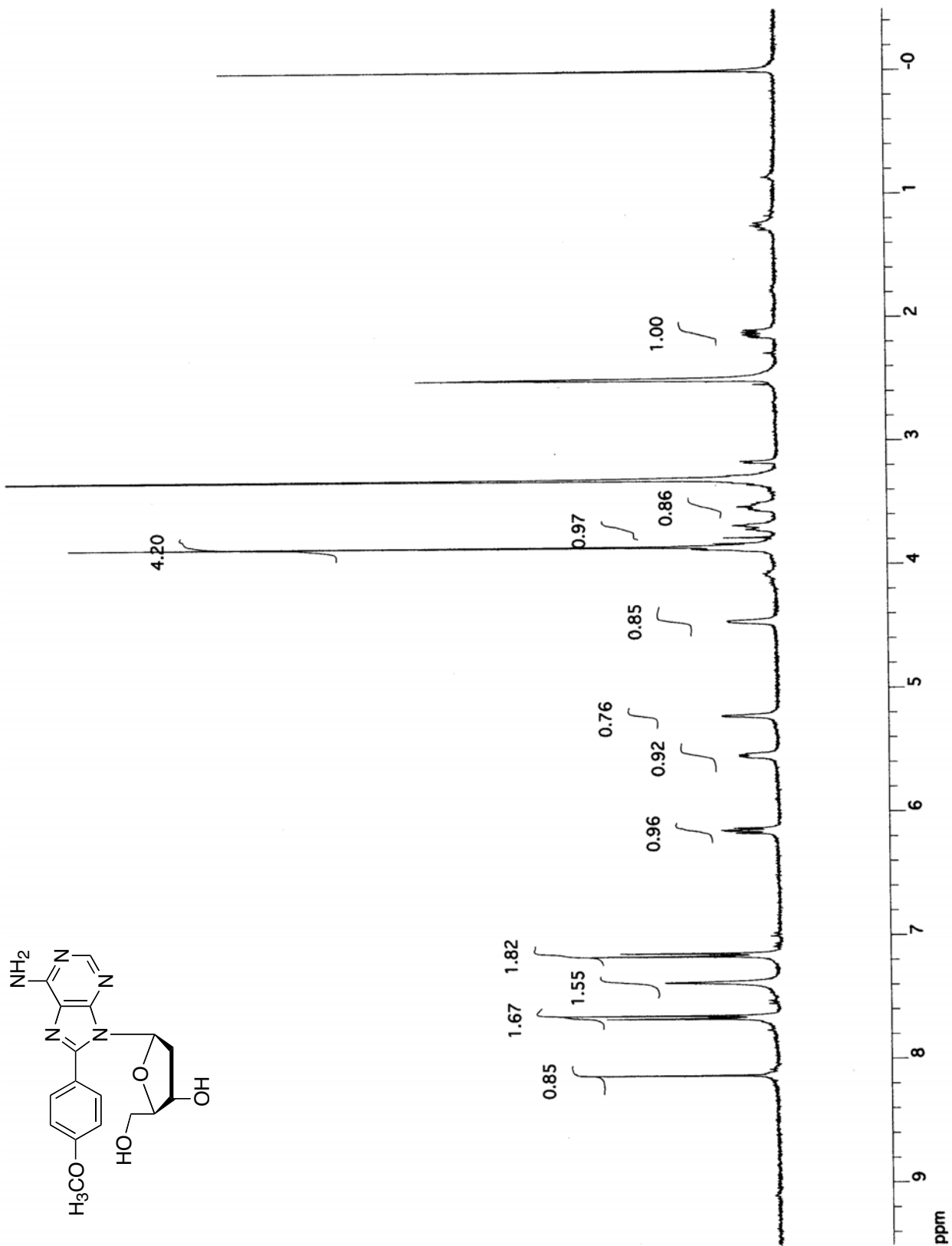
^{13}C NMR spectrum of 8-phenyl-2'-deoxyadenosine (5a)



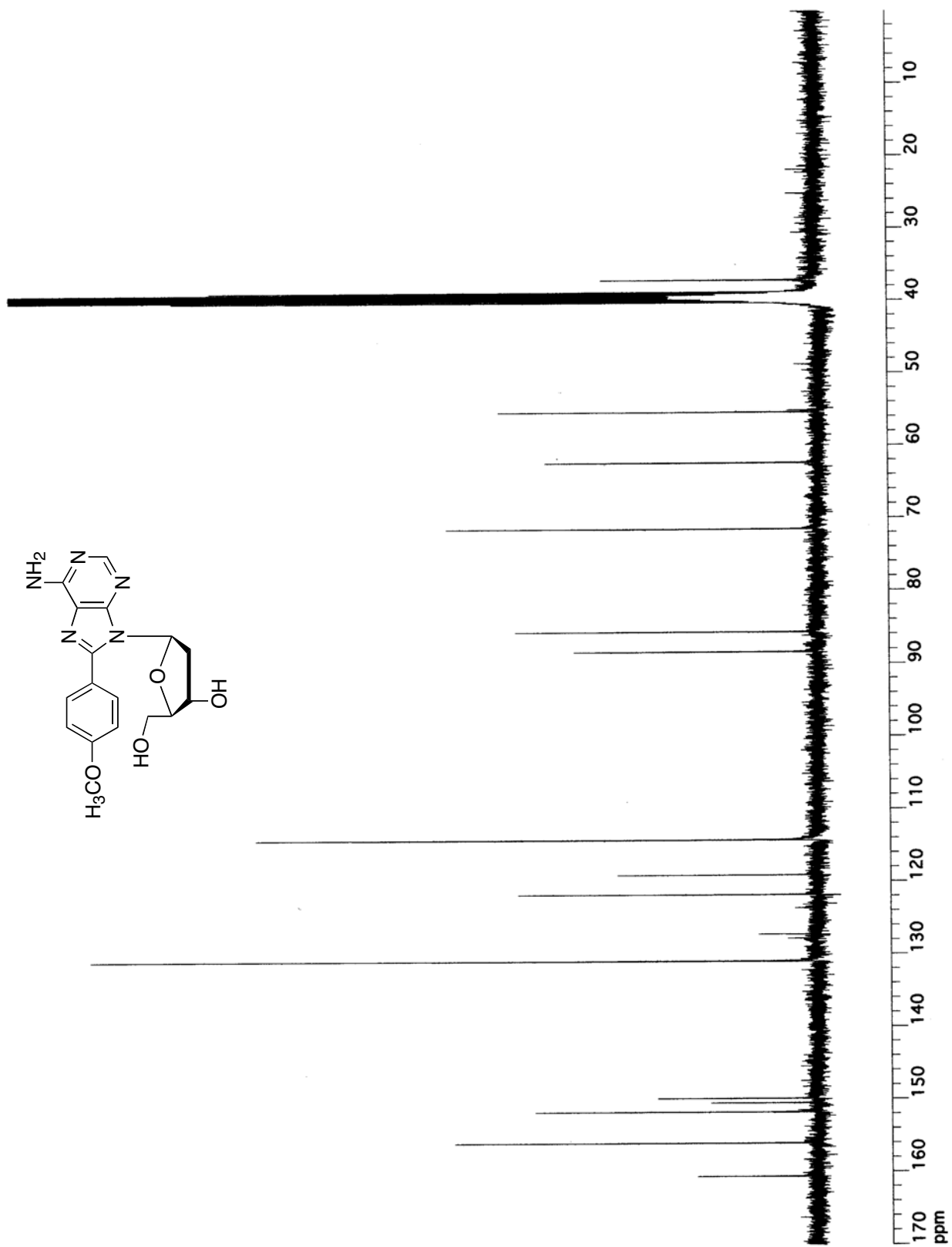
¹H NMR spectrum of 8-(4-tolyl)-2'-deoxyadenosine (**5b**)



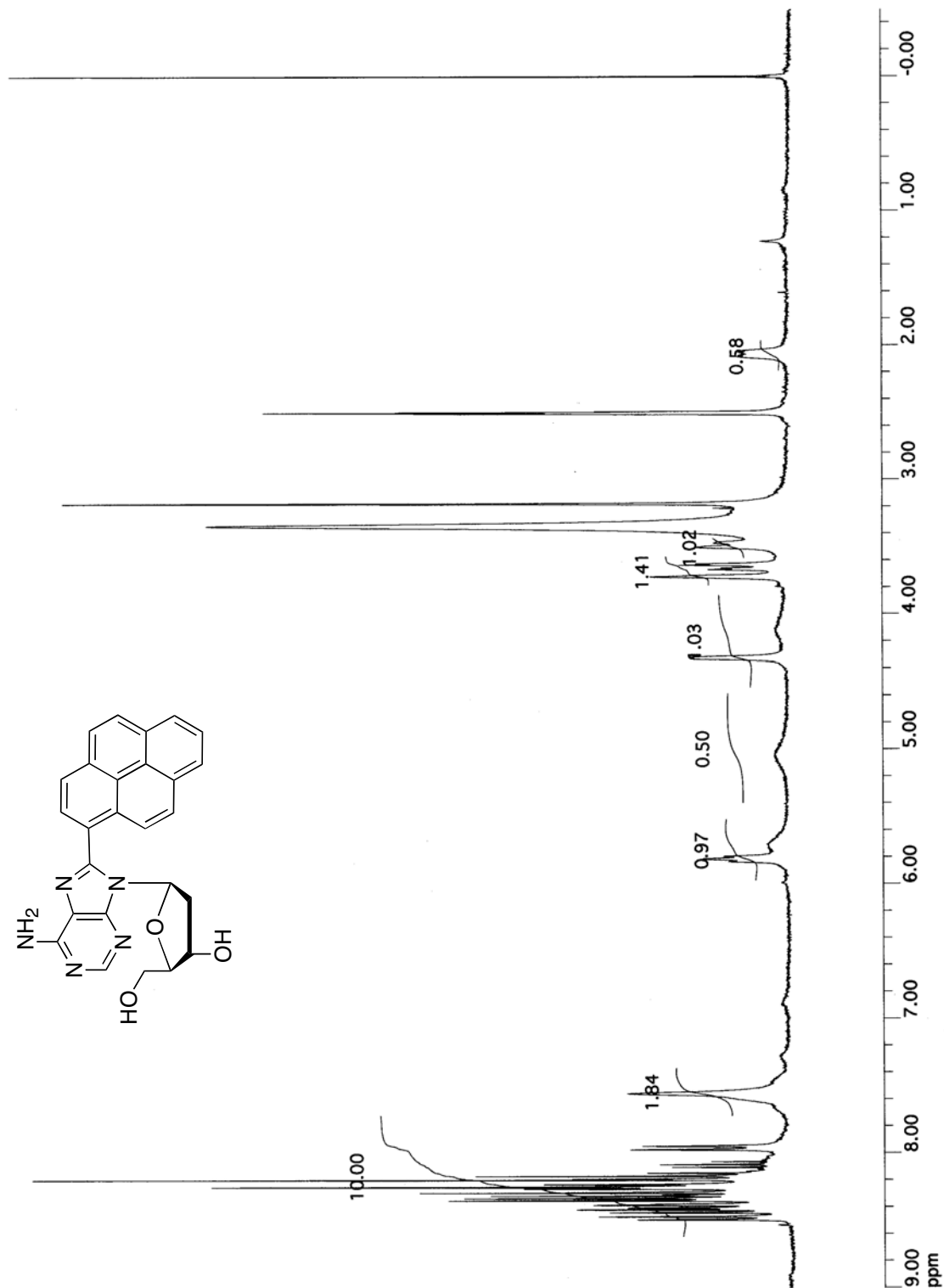
^{13}C NMR spectrum of 8-(4-tolyl)-2'-deoxyadenosine (**5b**)



¹H NMR spectrum of 8-(4-methoxyphenyl)-2'-deoxyadenosine (**5d**)

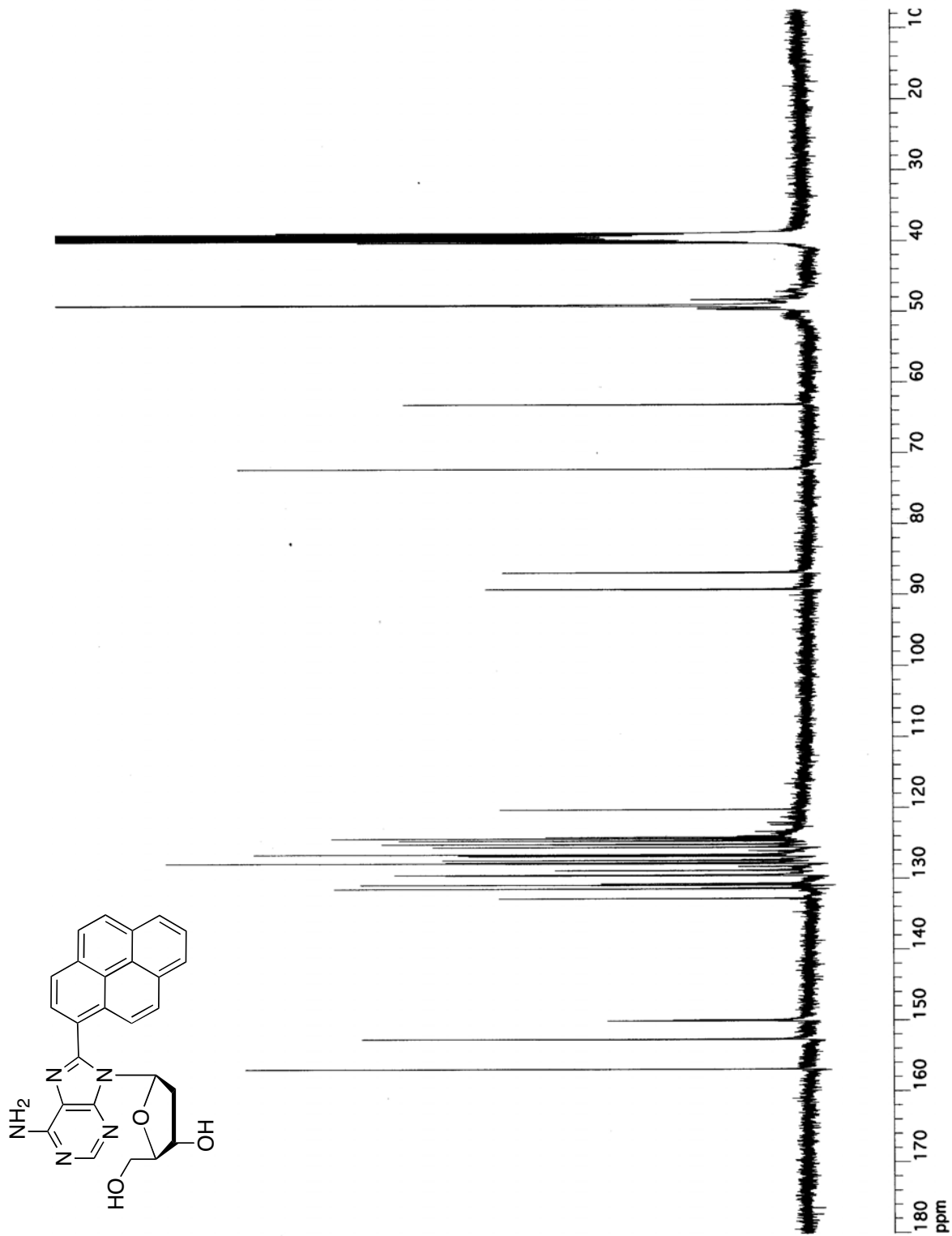


¹³C NMR spectrum of 8-(4-methoxyphenyl)-2'-deoxyadenosine (**5d**)



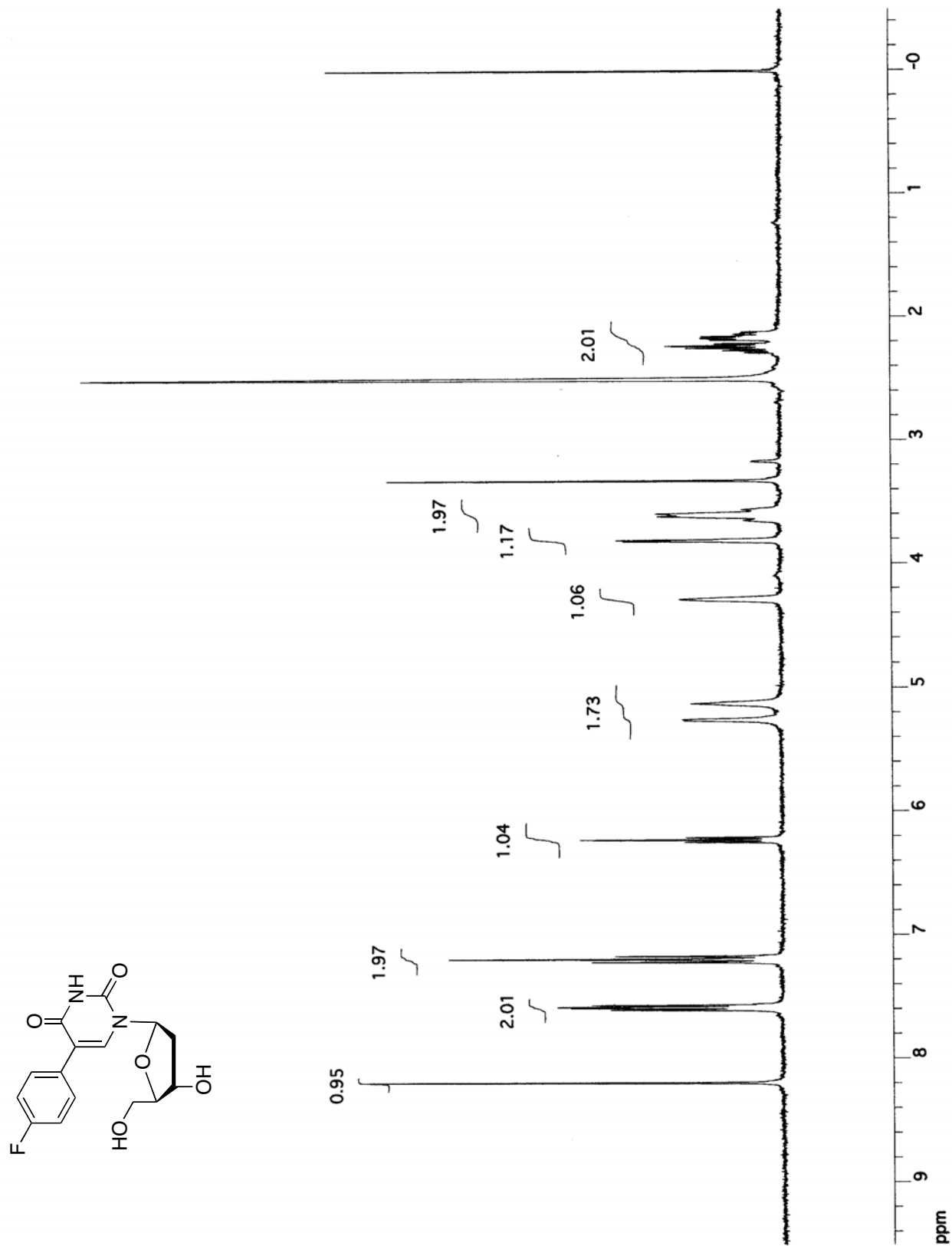
^1H NMR spectrum of 8-(pyren-1-yl)-2'-deoxyadenosine (5g)

Residual methanol at 3.18 ppm

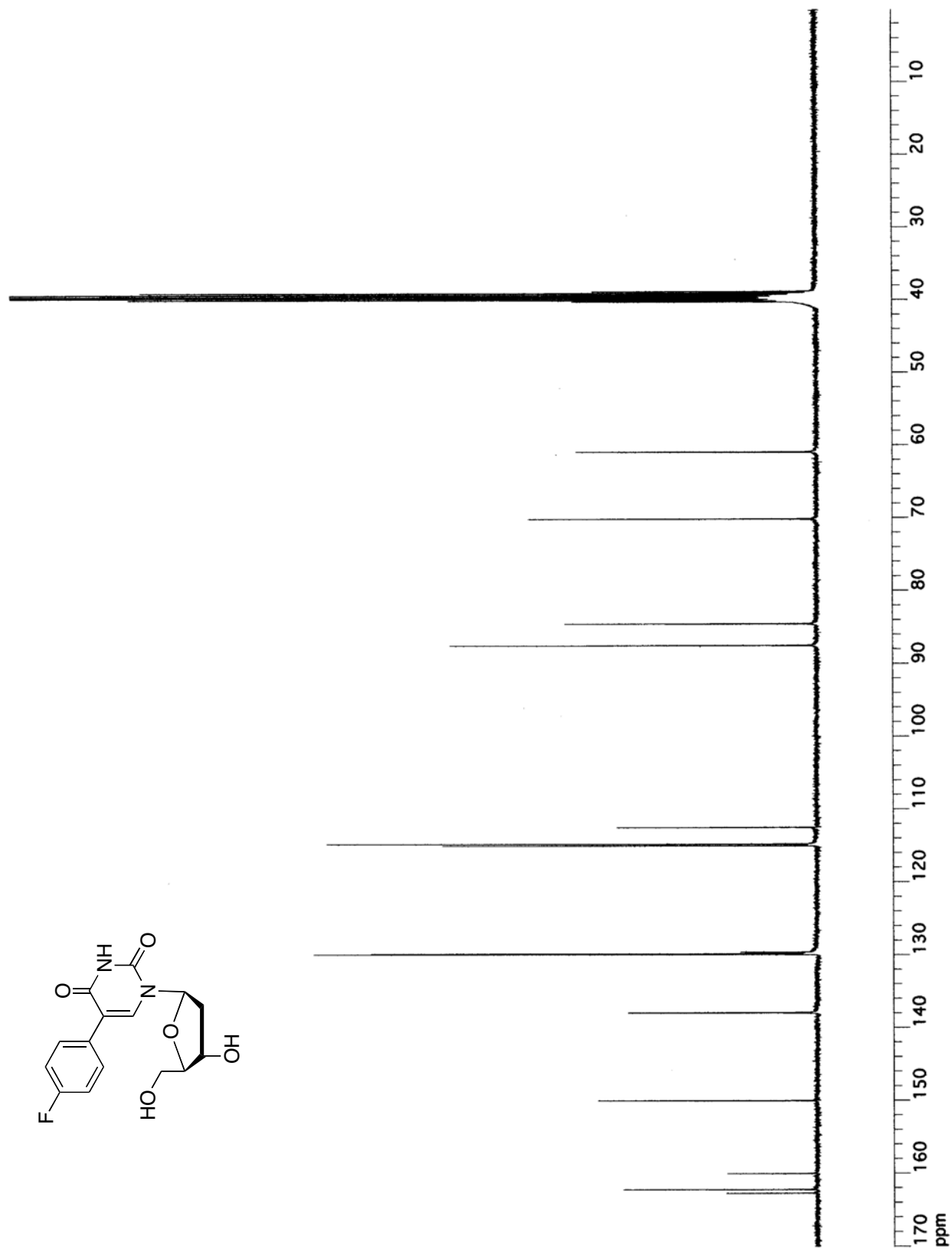


¹³C NMR spectrum of 8-(pyren-1-yl)-2'-deoxyadenosine (**5g**)

Residual methanol at 49.0 ppm



¹H NMR spectrum 5-(4-fluorophenyl)-2'-deoxyuridine (7e)



¹³C NMR spectrum 5-(4-fluorophenyl)-2'-deoxyuridine (7e)

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